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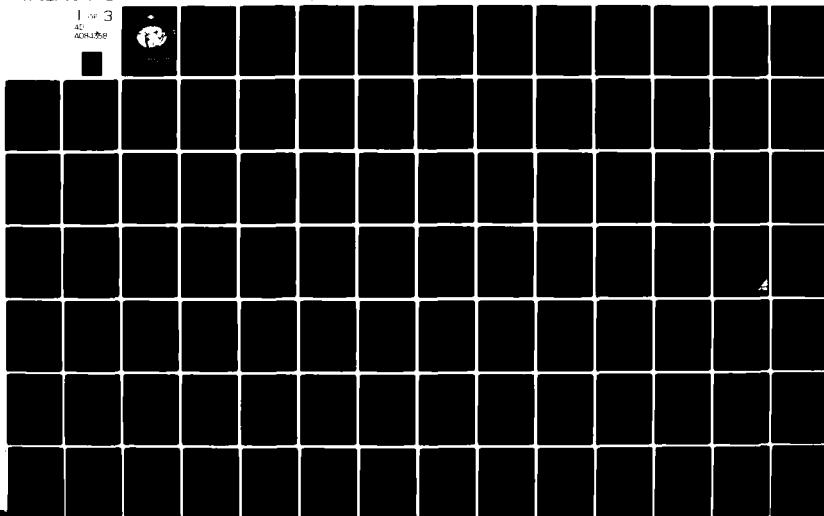
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19. ABSTRACT (Continue on reverse side if necessary and identify by block number) This report serves to detail the progress, status, and funding of approved projects conducted under protocol by staff members, interns, and residents at William Beaumont Army Medical Center. The varying projects as reported are classified according to the service or department to which the principal investigator belongs. Research conducted at WBAMC is categorized as either basic experimental medicine or trials and testing of clinical medicine procedures using the indigenous population for which this medical facility provides support.		

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FOREWORD

The Clinical Investigations Service, formerly Medical Research and Development, is entering its 15th year of operation. The Service continues to apply the best research principles and techniques available in an effort to obtain the most reliable results.

Budgetary and personnel turmoil and uncertainty persisted, but progress was realized in FY79. As always, the Clinical Investigations Service must continue to justify its existence. In respect to the latter, it remains appropriate to reiterate the policy and objectives as outlined in Department of Defense Directive Number 6000.4 dated 7 April 1971:

"Clinical investigation is an essential component of optimum medical care and consists of the organized inquiry into clinical health problems, for the following purposes:

1. To achieve continuous improvement in the quality of patient care.
2. To provide experience in the mental discipline achieved by participation in such organized inquiries, and to provide experience for personnel who will ultimately be teaching chiefs in military hospitals and medical specialty consultants.
3. To maintain an atmosphere of inquiry because of the dynamic nature of the health sciences.
4. To maintain high professional standing and accreditation of advanced health education programs."

In spite of limitations of funds and trained personnel compared to previous years, the Service has fulfilled its mission in a productive manner. The investigators who actively pursued their projects, frequently utilizing their own hours from off-duty time and occasionally providing their own funds, are to be especially commended. All investigators for each work unit are identified in the respective reporting sections.

The contributions of the many nurses, technicians, corpsmen and administrative personnel who are vital to the successful implementation of clinical research projects are acknowledged.

I am grateful for the editorial and typographical assistance of Ms Peggy Casteel in the completion of this document and to the remaining staff of the Service for their varied areas of contribution.



L.L. PENNEY, M.D.
LTC, MC
C, Clinical Investigations Service

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PREVENTIVE MEDICINE

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DEPARTMENT OF PSYCHIATRY

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DEPARTMENT OF SURGERY

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VETERINARY ACTIVITIES

Lumpkin WL, Coker ME, DeHaven WR: Gastric Ulcer in a Military Working Dog. Vet Med/Sm An Clin 9 Apr 79.

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UNIT SUMMARY

OBJECTIVES

The Clinical Investigations Service of William Beaumont Army Medical Center was established 2 February 1965 as the Medical Research and Development Service. The mission is to promote and coordinate clinical research and directed basic research. The Service supports in-house research projects by AMEDD staff members, residents, and interns, assisting in the formulation, preparation, and promulgation of research protocols and final research publications. The Service furnishes experimental design and statistical and technical expertise, develops and carries out special laboratory procedures, and provides general support in terms of equipment, supplies, and animal resources when necessary. The creative and inspirational environment and technical knowledge available serve to stimulate the undertaking of basic and clinical medical and paramedical research at William Beaumont Army Medical Center by staff members, and interns and residents in training, as well as provide a basic instructional facility to elucidate the principles and conduct of research.

In addition to the primary mission, as stated above, the Service is active in supporting several training and teaching programs involved with direct patient care. As examples, LT Klenke conducts a year-long health physics course supplemented with statistical review for the Nuclear Medicine Fellowship. LTC Penney provided a weekly statistics seminar for the perinatology fellowship. The Biological Research Facility directly supported approximately 150 anesthesia and surgical assistance training procedures ranging from minor suturing techniques for the Clinical Specialist Course students through aortic bypass grafts for the surgical residents.

TECHNICAL APPROACH

The Clinical Investigations Service provides support for staff research projects under the guidelines of the Declaration of Helsinki, Clinical Investigation Program (AR 40-38), and the Use of Investigational Drugs in Humans and the Use of Schedule I controlled Drug Substances (AR 40-7). Research is conducted under protocols approved by the Research Committee (WBAMC HR 70-4), the Human Use Committee (WBAMC HR 40-38) and the Radioisotope Committee (WBAMC HR 40-37) where applicable. In those research protocols utilizing laboratory animals, the investigators follow guidelines set forth in "Guide for Laboratory Animal Facilities and Care," published by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council, and the criteria established by the American Association for Accreditation of Laboratory Animal Care.

MANPOWER

Title	SSI/MOS	Auth	Assigned	Name
Chief	60J	0-5	0-5	Penney, Larry L., MC
Nuc Med Sci/ Admin Off	68B	0-5	0-1	Klenke, WJ, MSC
Biochemist/ Asst Chief	68E	0-3	0-4	Sellers, M.E. MSC
Vet Lab Animal Off	64C	0-3	0-3	Parker, G., VC
Med Lab Sp	01H20	E-5	E-6	Robinson, Bryan
Vet Anim Sp	91T20	E-3	E-4	Lee, Daniel F
Vet Anim Sp	91T10	E-3	E-4	Graf, James P
Vet Anim Sp	91T10	E-3	E-3	Lipp, Gary
Vet Anim Sp	91T10	E-3	E-3	Revels, Scott
Hlth Tech/ Ann Res Asst	00699	GS-7	GS-7	Revels, J.E.
Ann Caretaker	07706	WG-3	WG-1	Burton, A.D.
Chemist	01311	GS-11	GS-11	Rauls, D.O.
Microbiologist	00403	GS-11	GS-11	Frederick, R.
Chemist	01320	GS-9	GS-9	Sandison, S.W.
Chemist	01320	GS-9	GS-9	Meyers, T
Med Lab Tech	00645	GS-7	GS-7	Manna, B.S.
Med Lab Tech	00645	GS-7	GS-7	Teasley, C.E.
Editorial Asst	01087	GS-7	GS-7	Casteel, P.J.
Med Lab Sp	01H20	Recognized Requirement - Not Authorized		
Vet Ann Sp	91T10	"	"	" "

EXPENDITURES

	FY77&7T	FY78	FY79
Personnel (Civilian)	148,153	118,995	151,769
Consumable Supplies	56,831	35,923	34,392*
MEDCASE Equipment	40,324	33,169	37,333*
Capital Equipment	-	-	2,425
TDY	3,485	2,805	1,179
Contracts, Services, Printing and reproduction	4,327	3,053	937
TOTAL	\$ 261,120	\$193,945	\$228,035
Military Pay			141,385
			\$369,420

- *The above are comptroller figures. The CIS actually committed \$44,039 for consumable supplies and \$95,000 for MEDCASE in FY79. The differences will apparently be accounted against the Service in FY80. The CIS has further accounted the supply expenditures into general office \$2242; general laboratory (divided among 2 or more protocols or for maintenance, standards, etc.) \$15,383; and general biologic research facility (primarily training protocols) \$11,021. The remaining \$15,393 was spent on 19 specific protocols and the exact amount is noted under consumable supplies on the appropriate detail sheets.

It is impossible to account equipment, personnel, TDY and general supplies to specific protocols. However eliminating terminated protocols there were 92 active protocols in FY79. The following figures will be high estimates because a portion of personnel, supply, and equipment expense is for training as opposed to research. Furthermore all of the salary for the C, Clin Investigations Service is accounted here and a significant portion of his time is actually spent in patient care and teaching.

Using the Comptroller data listed above \$369,420/92 indicates an overall average of \$4,015 total expenditure per active protocol. Several of the older protocols received more limited funding in deference to those more current. It is also important to note that a large clinical study, with little or no equipment or laboratory expense, can be quite costly in terms of personnel for administration, data collection, and reduction, committee preparation, annual review, HSC and OTSG coordination and manuscript preparation. The average personnel cost for these services exceeds \$500 per protocol for the WBAMC, CIS. Partly due to the avalanche of regulations and increasing numbers of forms, minutes, etc., which must be maintained and distributed, the supply cost for paper, clips, staples, folders, and other strictly administrative materials have risen to an average of \$25 per protocol per year.

TDY for minimal continuing education and mission-essential training was granted. The Service provided only one TDY trip for an investigator to present findings at a professional meeting. The moratorium on minor equipment purchases was lifted and the Service also made major gains in MEDCASE including a research gamma counter, liquid scintillation counter, UV spectrophotometer, and medium speed centrifuge.

The Service had two recognized requirements unfilled in FY79, but all authorized positions were filled. The modest increase in numbers of protocols accepted and completed, and in publications and presentations attests to the value of stabilization as noted in last year's report. Stabilization of principal investigators continues to be a problem as witnessed partially by the number of terminated protocols.

During this fiscal year WBAMC authors had 46 articles or presentations published or accepted and submitted another 27.

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAILED SHEET

TITLE: Normal Values of Serum Triiodothyronine (T3) as Determined by
Radioimmunoassay in Various Clinical Euthyroid States

WORK UNIT NO: 75/07

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD; Douglas Daniels, DAC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Determine normal values of T3 for: (a) Pregnancy during all three trimesters. (b) Females taking oral contraceptives. (c) Euthyroid Hashimoto's Disease. (d) Other thyroiditides.

TECHNICAL APPROACH

Serum samples will be obtained from patients during 1st, 2nd, and 3d trimester of pregnancy; females on oral contraceptives for at least three months; euthyroid patients with Hashimoto's thyroiditis before treatment with thyroid hormone and after treatment with Synthroid; patients with thyroiditis (subacute). Clinical histories will be obtained and the clinical thyroid state will be determined. The serum samples obtained will be evaluated by radioimmunoassay. Determination of the inclusion into the proposed categories will be from clinical diagnosis, clinically determined thyroid state and appropriate laboratory studies.

PROGRESS

Papers have been published in Clinical Nuclear Medicine reporting studies of T3 values in pregnancy and in patients with chronic renal failure on dialysis. Studies in other euthyroid states are ongoing but have been limited due to funding constraints.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Isolation and Purification of Choline Phosphotransferase

WORK UNIT NO: 75/30

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To develop a method for the isolation of choline phosphotransferase from lung tissue and correlate respiratory distress with the presence and specific activity of this enzyme.

TECHNICAL APPROACH

Microsomal and lysosomal fractions of lung tissue will be subjected to standardized enzyme purification techniques. Cofactor effects will be studied in order to assess possible prophylaxis development in cases of respiratory distress.

PROGRESS

This protocol has been suspended but may be resumed if the budget allows. The previous principal investigators began to characterize CPT from rabbit fetal lung. A portion of that work investigated enzyme activity under the influence of corticosteroids. A manuscript submitted in FY79 is excerpted below:

All subject groups were composed of pregnant New Zealand white rabbits of known gestation, purchased from a commercial research animal supplier and acclimatized in our research laboratory for a minimum of one week. An initial group of rabbits served to establish an index of normal CPT activity at various gestational ages; one or two members of this group were sacrificed when gestation was 70% to 100% complete, and the levels of CPT activity in the fetal lung tissue and the amniotic fluid were measured. Then three groups of rabbits were treated when gestation was 80% complete: the first, a group of 48, received 1.0 ml of isotonic saline intravenously; the second, a group of 56, 20 mgm/kg of hydrocortisone intravenously; and the third, a group of 59, 1.0 mgm/kg of betamethasone intramuscularly. Half of the rabbits in each of these three groups were sacrificed 12 hours after treatment via carbon dioxide euthanasia; the remaining rabbits were sacrificed 24 hours after treatment. Amniotic fluid was collected by needle aspiration, and the lungs from fetuses were removed in caud. Visible blood, fluid and remaining fetal materials were discarded. The amniotic fluid and the lungs from each litter were pooled separately.

The lung tissue was washed three times in isotonic saline and then homogenized as a 10% solution in 0.05 M tris HCl, pH 8.5. This suspension was centrifuged at 1200 g for 20 minutes; the supernatant was then withdrawn and centrifuged at 12,500 g for an additional 20 minutes. The amniotic fluid was centrifuged at 1650 g for five minutes. Three assays were performed on each sample of amniotic fluid and lung tissue using 0.8 ml of the supernatant for each assay.

The reaction medium for both fetal lung tissue and amniotic fluid enzyme activity was constituted according to the following modification of the Zachman procedure.

Component	Concentration	Volume(ml)
Amniotic fluid or Lung Enzyme	Varied	0.8
Dipalmitic (a,b-diglyceride)	$1.15 \times 10^{-3} M$	1.0
MgCl ₂		
CPD-Choline and CPD ¹⁴ C-Choline	(p.04uC)	1.0

The fetal lung and amniotic fluid preparation were incubated in this medium under constant agitation (at 37°C) for two hours, at which time the reaction was terminated by the addition of 0.5 ml of 10% trichloroacetic acid. Then, 1.5 ml of butanol were added; this solution was first shaken for 30 minutes at ambient temperature and then centrifuged for 10 minutes at 12,500 g. After centrifuging, 0.5 ml of the butanol phase supernatant was transferred to a liquid scintillation vial containing 2.0 ml of ethoxyethanol and 10.0 ml of scintillation fluid (toluene-PPO and POPOP). Using a Beckman model 1650 liquid scintillation system precalibrated for ¹⁴C., the enzyme activity of each sample, expressed as counts per minute per gram of protein, was measured over a five minute period; each sample was counted three times.

Results

When fetal lung samples from litters at 70% to 100% gestational age were tested for CPT activity, no significant increase was found with advancing gestation. It was noted that if the CPT activity was expressed as counts per minute per milliliter, amniotic fluid samples for the same period had a three-fold higher CPT activity later in pregnancy. However, the amniotic fluid protein for this period was increased five-fold; this results in no increased CPT activity when expressed as counts per minute per gram of protein.

The CPT activity of fetal rabbit lungs was significantly increased at 12 and 24 hours in the groups receiving cortisol or betamethasone when compared with the group receiving saline. There was no significant difference between the cortisol and the betamethasone treated groups.

Several clinical states, including hypertension and chronic abruption, are believed to be associated both with accelerated fetal lung development in humans and with increased fetal cortisol production. While thyroxine, epidermal growth factor, adrenocorticotrophic hormone, and xanthines have also been noted to enhance lung maturation, only the corticosteroids have been used in clinical trials.

This study documents a significant increase in fetal lung choline phosphotransferase activity, an important enzyme in the production of surface-active phosphatidyl choline, upon the maternal injection of corticosteroids. This increased activity may result either from an increased availability of substrates or from an actual increase in enzyme activity. The discrepancies between our findings and those of studies reporting no such significant increase may be explained by differences in experimental design. Previous animal studies involved anesthetics and surgical manipulations during the direct injection of fetuses. The surgical and anesthetic procedures used by Rooney induced a three-fold increase in fetal lung CPT activity before any corticosteroids were administered. The resulting anesthetic and operative stresses may have resulted in increased endogenous corticosteroid activity which of itself provided maximal stimulation of the fetal lung choline phosphotransferase activity and rendered superfluous the effects of exogenous corticosteroids.

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Variables in the Measurement and Calculation of MTF

WORK UNIT NO: 78/09

PRINCIPAL INVESTIGATOR CPT A.R. Benedetto

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To assess exhaustively the impact of asymmetric line source response functions on determination of modulation transfer function.

TECHNICAL APPROACH

Asymmetric line source response functions whose kurtosis and skewness are known will be used to calculate modulation transfer function (MTF). The resulting MTF curves will be analyzed to determine what degree of asymmetry is acceptable for gamma camera quality control.

PROGRESS

Resignation of the principal investigator precluded further work on this project.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DEPARTMENT

TITLE: Theoretical and Applied Techniques in Gamma Camera
Uniformity Quality Control

WORK UNIT NO: 78/21

PRINCIPAL INVESTIGATOR 2LT W.J. Klenke, MSC

ASSOCIATE INVESTIGATORS: LTC W.F. Kendall, MSC

OBJECTIVES

To develop the theoretical, mathematical basis for defining the separation distance between a gamma camera and a point source for which exposure variations across the face of the gamma camera are reduced to a statistically insignificant level.

TECHNICAL APPROACH

A computer program will be used to calculate the exposure rate at each location on a grid imposed on the face of standard and large crystal gamma cameras for varying separation distances between the point source and the camera. The effect of off-axis alignment of the source will also be evaluated. Experimental confirmation of the computer results will be obtained, using transmission densitometry to measure exposure variations.

CONSUMABLE SUPPLIES

\$100

PROGRESS

Computer calculations indicated that separation distances between gamma cameras and point flood sources need to be greater than those in general use in clinical nuclear medicine. Preliminary results were presented at the Southwestern Chapter, Society of Nuclear Medicine, 17 Mar 79. Further calculations are being performed preparatory to submission of a manuscript for publication. A summary of the presentation follows:

Sensitivity nonuniformity correction methods currently in use require exposure of the crystal to a uniform flux of photons in order to establish a mathematical variation-smoothing algorithm. The separation distance of a point source used to approximate a planar flood source must be sufficient to insure that deviations in exposure across the face of the detector due to the nonparaxial nature of the incident photon beam are within acceptably small limits ($\pm 2-3\%$). These deviations are sensitive to the diameter of the camera crystal, the source-crystal separation distance, and the amount by which the source is imperfectly centered. Data were presented to illustrate the effects of varying source-detector separation distances and improper source centering, using a representative selection of small and large crystal camera. For the large crystal cameras, deviations across the crystal with the source centered were shown to be on the order of 3.0 - 4.2% at one meter, 0.8 - 1.1% at two meters, and 0.3 - 0.5% at three meters; for the small crystal cameras, the corresponding deviations are 1.7%, 0.4%, and 0.2%, respectively. With the source centered on the edge of the detector (worst credible case), the large crystal cameras exhibit deviations of 10.9 - 15% at one meter, 2.9 - 4.2% at two meters, and 1.3 - 1.9% at three meters; for the small crystal cameras, the corresponding deviations are 6.3%, 1.7%, and 0.8%, respectively. The importance of minimizing these deviations was shown to be especially important when computerized quantitative analysis was to be performed.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Significance Study of meta and para metabolites of
Catecholamine Compounds in the Rat

WORK UNIT NO: 78/28

PRINCIPAL INVESTIGATOR: MAJ M.E. Sellers, 'SC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the significance of meta and para substituted isomers of catecholamine metabolites such as m- and p-tyramine and m- and p-phenylacetic acids by noting changes in isomer quantitation after selective inhibition of the normal metabolic pathway.

TECHNICAL APPROACH

Weanling male Sprague-Dawley rats will be divided into test and control groups. Test animals will be injected with various regimens of catecholamine enzyme inhibitors as well as exogenous L-DOPA. Catecholamines and their acid metabolites will be determined by GC, GOS, TLC, etc. As many meta- and para-isomers will be identified, separated, and quantitated as is possible from brain, liver, and urine extracts. The data will be compiled to ascertain whether metabolic inhibition of normal pathways changes the ratios of meta- and para- metabolites and to try to investigate the significance of these changes if they occur.

CONSUMABLE SUPPLIES

\$200

PROGRESS

Meta and para metabolite standards have been purchased. Metabolic rat cages have arrived, so animal studies will begin early in FY80. Standards are being evaluated by GLC to determine retention time data as well as column and derivitization evaluation.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

Quantitative and Qualitative Phenolic Acid Changes in Rats
TITLE: Treated with Catecholamine Pathway Inhibitors

WORK UNIT NO: 78/29

PRINCIPAL INVESTIGATOR: MAJ M.E. Sellers, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Acid metabolites of L-DOPA, i.e., homovanillic acid (HVA), dihydroxyphenylacetic acid (DOPAC), Vanilmandelic acid (VMA), p-hydroxyphenylacetic acid, m-hydroxyphenylacetic acid, and p-hydroxymandelic acid will be qualitatively measured in urine of rats pretreated with monoamine oxidase inhibitors, and B hydroxylase inhibitors, then treated with radioactive (^{14}C) L-DOPA. The purpose of this study is to determine the effect of catecholamine pathway inhibitors on end metabolism acids.

TECHNICAL APPROACH

Weanling rats will be divided into test and control groups. Test animals will be subjected to various regimens of catecholamine pathway inhibitors such as B hydroxylase, monoamineoxidase, and decarboxylase inhibitors. Endogenous catecholamine metabolite acids will be measured in urine and compared to control animals. Exogenously administered radioactively (^{14}C) labeled L-DOPA will be given to both test and control animals and again acid metabolites will be measured in rats urine and compared to control animals. Urinary catecholamine acids will be measured by current techniques including gas chromatography, thin layer chromatography, etc. Scintillation counts will be performed on each acid fraction. Determinations and conclusions will be made from comparing endogenous and exogenously labeled metabolites by paying careful attention to changes in specific activity and quantitation changes after exogenous L-DOPA injections. Catecholamines may also have to be determined in order to study feedback inhibition and metabolic pathway shunt studies.

CONSUMABLE SUPPLIES

\$284

PROGRESS

Metabolic rat cages have just been received so animal studies will begin early in FY80. All standard compounds and derivatives have been purchased. Standardization data is being collected via GLC.
STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM B. FAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Minor Amine Metabolites of L-DOPA

WORK UNIT NO: 78/30

PRINCIPAL INVESTIGATOR: MAJ M.E. Sellers, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Weanling male rats will be injected with altered L-DOPA.
Metabolism will be studied in the rat model.

TECHNICAL APPROACH

Forty male weanling Sprague-Dawley rats will be divided into four groups. The ten animal control group will be fed normal rat TEKLAB diet. Thirty animal test groups will have methionine supplement either by intubation or mixed with the TEKLAB pellets. The animals will be kept on this diet for ten days. Test animals will be further broken down into three groups of ten animals. Animals will be sacrificed at intervals starting at 2-24 hours after L-DOPA injection. Urine will be collected during this time. Brain, liver, and urine will be extracted for N- and O-methylated amines. They will be quantitatively and qualitatively determined by GC, GC/MS, TLC, LC, etc.

CONSUMABLE SUPPLIES

\$94

PROGRESS

L-DOPA metabolites have been purchased. Standardization and extraction technique as well as derivitization techniques are being investigated by GLC. Metabolic rat cages have just arrived so animal studies will begin in FY80.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Role of Deoxyribonucleic Acid Attachment to Cell Membrane
in the Regulation of Bacterial Growth

WORK UNIT NO: 79/01

PRINCIPAL INVESTIGATOR: Robert Frederick, PhD, DAC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To isolate and examine specific deoxyribonucleic acid (DNA) sequences associated with bacterial cytoplasmic membranes.

TECHNICAL APPROACH

Our initial experiments are designed to analyze the effect of different restriction enzymes on isolated nucleoids. These are the folded chromosome of the bacteria which can be isolated in their compact state while retaining the membrane association [5]. The procedure can be done simply with reasonable yields under salt and pH conditions which will facilitate endonuclease treatments. Once isolated, the tritium labeled nucleoids (i.e. the entire chromosomes) will be digested with commercially available restriction endonucleases. These enzymes cleave the DNA molecules at specific nucleotide sequences resulting in specific fragments which can subsequently be separated by agarose gel electrophoresis and resolved on x-ray film by autoradiofluorography. Membrane associated fragments will be purified by fractionation using the magnesium-sarkosyl crystal separation technique [6]. The fragments will be recovered by standard techniques and analyzed by agarose gel electrophoresis. Once the specific sequences have been resolved, we will begin to identify what regions of the chromosome are involved and under what conditions. The relationship of the attachment to bacterial growth may then be examined by varying the growth conditions of the organisms, using appropriate mutant strains and in the presence of various antibiotics.

CONSUMABLE SUPPLIES

\$2131

PROGRESS

An abstract was presented at the annual meeting of the American Society for Microbiology in Los Angeles, CA and is detailed below:.

DNA attachment to the membrane allows the provocative notion that this interaction may have a regulatory basis. A procedure has been developed to visualize DNA fragments associated with the membrane. Escherichia coli nucleoids were isolated and digested with the restriction enzyme Eco RI. Membrane associated fragments were isolated by the Magnesium-Sarkosyl (M-Band) technique in sucrose gradients and analyzed on 0.6% agarose gels. The amount of DNA sedimenting with the M-Band fraction was dependent upon the volume of crystals added, with 23 to 35% of the total DNA cosedimenting at the higher levels. When these DNA fragments were recovered and analyzed on agarose gels they were enriched for several bands not seen in the total digest samples. These data suggest that unique regions of the DNA are associated with the membrane.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SUMMARY

Synthesis of Inhibitors of the Shikimate Pathway for Investigation
TITLE: As Potential Antimicrobial Agents

WORK UNIT NO: 79/07

PRINCIPAL INVESTIGATOR: David Rauls, PhD, DAC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The 6-alpha and 6-beta fluoro analogs of shikimic acid will be synthesized as potential irreversible inhibitors of the pathway responsible for aromatic acid synthesis in microorganisms. The compounds will then be evaluated for antibacterial activity using a standard antibacterial screen.

TECHNICAL APPROACH

The desired 6-fluoro analogs of shikimic acid will be synthesized by established synthetic techniques. The antimicrobial activity will be determined using standard assays. The anticipated limiting factors appear to be related to the potential lability of the products.

CONSUMABLE SUPPLIES

\$366

PROGRESS

The shikimic acid molecule contains acid and hydroxyl groups that must be protected in order for the desired product to be formed. To date, work has involved preparation of the appropriately protected molecule in preparation for the final reaction sequence. The fully protected molecule has been synthesized and future work will involve preparing additional quantities of the protected shikimic acid followed by attempts to brominate and fluorinate the molecule.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Analysis of the Histologic Soft and Bony Tissue Effect
of Terra Cortril Healing Dental Extraction

WORK UNIT NO: 78/17

PRINCIPAL INVESTIGATOR MAJ B. J. Klinger, DC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the histologic soft and bony tissue response to
Terra-Cortril (Tetracycline - 30 mg and Hydrocortisone -
10 mg/gm).

TECHNICAL APPROACH

Using a dog model for surgical removal of selected mandibular
teeth and placement of Terra-Cortril in one side only. The
opposite side is to act as the control. The animals are to be
sacrificed at predetermined intervals, the mandibles resected
and microscopic examination of the extraction sites.

PROGRESS

The animals were all treated and plasma cortisol was measured. They
were sacrificed but the histology laboratory dessicated specimens
excessively. The principal investigator was reassigned and the
project has been terminated.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Holographic Analysis of Stress Produced in a Pier Abutment Fixed Partial Denture

WORK UNIT NO: 79/08

PRINCIPAL INVESTIGATOR: LTC R.T. Brown, DC

ASSOCIATE INVESTIGATORS: MAJ T.S. Strain, MAJ R.R. Larson

OBJECTIVES

To demonstrate the distribution of stress in rigid and non-rigid pier fixed partial dentures with the use of holographic birefringence. To demonstrate the usefulness of the hologram as a stress measuring instrument in prosthetic dentistry and to unequivocally prove the need for nonrigid connectors in pier abutment fixed partial dentures.

TECHNICAL APPROACH

Outline of phases of investigation: A five-unit pier fixed partial denture will be fabricated using rigid connectors. A holograph will be made of the FPD in an unstressed mode. The FPD will be stressed with forces from 1-21 lbs in increments of 2 lbs. The point stress will be placed over each abutment individually, as in an ideal occlusion, with the points in central fossas and with a bolus of food. Holograms of the model in the stressed mode will be superimposed over the unstressed mode and the birefringence will be recorded on film. The same procedure will be carried out using a five-unit pier fixed partial denture fabricated using a nonrigid connector.

PROGRESS

Filters for the laser holograph required to complete the study have been purchased but not delivered.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Antibiotic Prophylaxis in Intraoral Orthognathic Surgery

WORK UNIT NO: 79/09

PRINCIPAL INVESTIGATOR: MAJ J.E. Ruggles, DC

ASSOCIATE INVESTIGATORS: COL J.R. Hann, DC

OBJECTIVES

To conduct a prospective double-blind comparison of two prophylactic antibiotic regimens in patients undergoing intraoral orthognathic surgery of the maxilla and/or mandible.

TECHNICAL APPROACH

Drugs to be administered in the study are Procaine Penicillin G and Aqueous Penicillin G.

a. Aqueous Penicillin G is the antibiotic agent of choice for almost all infections originating in the oral cavity, and consequently, almost all infections resulting from intraoral orthognathic surgery.

b. Some controversy exists concerning what constitutes an appropriate period for prophylaxis.

(1) Peterson and Booth, in a retrospective study of patients undergoing intraoral orthognathic surgery, reported an 11.4% incidence of postoperative infection in patients who received prophylactic antibiotics, and an 11.1% incidence of postoperative patients who received no antibiotics.

(2) In a retrospective study by Yrastorza, the incidence of postoperative infection in patients undergoing intraoral orthognathic surgery was smaller in patients receiving no prophylactic antibiotics than for patients who received antibiotics for an average of eight days postoperatively.

(3) Zallen and Black presented what they termed current thoughts regarding the use of prophylactic antibiotics in orthognathic surgery. They recommended the use of antibiotics, but gave no recommendations concerning duration of coverage, and presented no statistical information to support their views.

(4) Burk presented guidelines for prophylactic antibiotic coverage in surgery, in which he advocates use of antibiotics only during the immediate postoperative period. However, no statistics were presented.

(5) To our knowledge, a prospective, double-blind study comparing short term and longer term prophylactic antibiotic coverage for intraoral orthognathic surgery has not been reported.

Patients eligible for inclusion in the study must be adults eighteen years of age and older, may be of either sex, and may be civilian or military.

Patients will be excluded from the study if they give a history of allergic reaction to penicillin or other Beta Lactam antibiotic, if they have a compromised immune defense system, or if they have received antibiotic therapy within the previous fourteen days.

Total numbers of patients will be forty, divided into two groups of twenty patients.

Antibiotic Regimens:

- (1) All patients will receive
 - 600,000 units Procaine Penicillin G and 400,000 units Aqueous Penicillin G, I.M., one hour preoperatively.
 - 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes every three hours intraoperatively.
 - 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes three hours after the last intraoperative dose.
- (2) Group I (20 patients) will receive
 - 2,000,000 units Aqueous Penicillin G, I.V. over 30 minutes every four hours for a total of twelve doses.
- (3) Group II (20 patients) will receive
 - A placebo I.V. over 30 minutes, every four hours for a total of twelve doses.

Method of Followup: Followup will consist of routine postoperative care, to include observation for signs of postoperative infection. The diagnosis of postoperative infection will be made if three of the following criteria are met:

- (1) Elevation of body temperature for longer than 72 hours postoperatively.
- (2) Increased edema, induration, and erythema of wound margins and surrounding tissue.

(3) Drainage of purulent exudate from the wound.

(4) Positive serial blood cultures.

Postoperative infections, once diagnosed, will be treated with local measures and the appropriate antibiotic(s) based upon culture and sensitivity results.

All infections will be cultured utilizing both aerobic and anaerobic methods.

PROGRESS

Approval from HSC was received 23 June 1979. Patients have been entered, but data is not yet available.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: $^{99m}\text{Tc-Sn-DTPA}$ Chelate in the Detection of Vesicoureteral Reflux

WORK UNIT NO: 75/24

PRINCIPAL INVESTIGATOR MAJ A. Hughes, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the usefulness of $^{99m}\text{Tc-Sn-DTPA}$ chelate as a renal imaging agent, and particularly in the demonstration of vesicoureteral reflux.

TECHNICAL APPROACH

Patients with known or suspected vesicoureteral reflux will be studied with $^{99m}\text{Tc-Sn-DTPA}$. The results obtained will be compared with clinical findings, laboratory tests, and roentgenographic studies. Commercially available radiopharmaceutical Sn DTPA preparation kits will be employed. The kits will be supplied by Diagnostic Isotopes, Inc., 123 Pleasant Ave., Upper Saddle River NJ. These kits are supplied in sterilized and pyrogen-free form. Other suppliers will be sought only if their product appears to be far superior and only from those manufacturers who have filed an IND with the Food & Drug Administration.

PROGRESS

None

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEALMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

1 TAIL SHEET

TITLE: Myocardial Perfusion Scanning with Radioactive Particles

WORK UNIT NO: 76/14

PRINCIPAL INVESTIGATOR MAJ A. HUGHES, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To demonstrate myocardial perfusion at the capillary level as an aid in differentiating those patients who are likely to benefit from coronary artery surgery. The injection of radioactive particles in each coronary artery will demonstrate runoff perfusion. This will provide supplemental information to determine candidates for coronary artery surgical procedures.

TECHNICAL APPROACH

Tc-99m microspheres and I-131 macroaggregated albumin will be injected into the left and right coronary artery respectively at the time of cardiac catheterization. Imaging will be performed with a gamma camera and the images will be studied for areas of decreased perfusion.

PROGRESS

Refer to FY78. This study has assumed the stature of a clinically acceptable tool and is no longer considered a research protocol.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

D. TAIL SHEET

TITLE: Effect of a Broad Spectrum Antibiotic on the Course of Viral URI

WORK UNIT NO: 76/23

PRINCIPAL INVESTIGATOR LTC R.E. Morrison, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine in a controlled double-blind study the effect of an antibiotic on the clinical course of acute viral upper respiratory tract infections with particular attention to any beneficial or deleterious effects of the treatment with respect to secondary bacterial complications.

TECHNICAL APPROACH

Patients admitted to the Acute Respiratory Distress (ARD) Ward without obvious bacterial infections were to be divided into two random groups. One group to receive tetracycline HCL, the other a placebo. The physician taking care of the patients, and the patients themselves, would not know whether they were receiving drug or placebo. The code would be held by the Pharmacy Service. The incidence of complications, in particular, secondary bacterial infections; the total length of fever; the general well-being; length of hospital stay; incidence of adverse drug reaction; and the total cost of treatment would be compared between the two groups.

PROGRESS

Staffing shortages have also caused suspension of this study. Another attempt to institute it with the next URI season is anticipated.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Diagnostic Adrenal Scanning with ^{131}I (NP59)

WORK UNIT NO: 76/33

PRINCIPAL INVESTIGATOR LTC T. Brown, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this study is to determine the usefulness of ^{131}I -NP59 in scanning of the adrenal glands. It will be employed for the following purposes: (a) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma, (b) imaging of adrenals in patients who require adrenal venography and are allergic to contrast media, (c) detection of unilateral adrenocortical hypofunction: calcification, metastatic carcinoma, post-venography infarction, etc., (d) detection of functioning adrenal remnant after adrenalectomy for Cushing's syndrome, (e) aid in assessment of adrenocortical steroid therapy.

TECHNICAL APPROACH

Patients with clinical evidence of adrenal disease will be studied upon referral from the Endocrine Service. Adrenal imaging will be performed after injection of the material to assess the presence or absence of visualization of the adrenal glands, their size and response to suppression therapy.

PROGRESS

NP59 appears to be a satisfactory agent for adrenal imaging and studies will be continuing with a new principal investigator.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Liver Amylase: Fact or Fiction

WORK UNIT NO: 77/07

PRINCIPAL INVESTIGATOR CPT L M Lehrner, MD

ASSOCIATE INVESTIGATORS: MAJ C M Lund, MD, LTC J S Gunther, MD

OBJECTIVES

The two objectives are: (1) to determine if human liver contains an α -amylase other than that contributed by "trapped" blood, (2) to determine if there is a detectable alteration in serum and/or urine total and amylase activity and/or amylase isozyme patterns in patients with liver disease.

TECHNICAL APPROACH

Routine laboratory examinations will be performed prior to each peritoneoscopy procedure. Depending on the clinical indications one or more liver biopsies will be obtained. A 5 mm core of liver tissue from each biopsy will be subjected to special assay, and accordingly the existence of liver amylase and alterations in serum and/or urine total amylase activity and/or amylase isozyme patterns in patients with histologically proven liver disease will be definitely proven or disproven.

PROGRESS

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

TAIL SHEET

TITLE: Radionuclide Angiocardiology Evaluation of
Cardiopulmonary Function Using a Mobile Dual Cardiac Probe

WORK UNIT NO: 77/16

PRINCIPAL INVESTIGATOR Robert Sonneraker, MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To assess the clinical usefulness of a mobile dual cardiac probe in the assessment and serial evaluation of cardiopulmonary function in patients with acute, chronic or potential cardiopulmonary compromise.

TECHNICAL APPROACH

Patients undergoing cardiac evaluation for a wide variety of clinical problems were studied to determine left ventricular ejection fraction, pulmonary transit time, cardiac output, stroke volume, end-diastolic volume and pulmonary blood volume at bedside.

PROGRESS

The mobile dual cardiac probe was used to evaluate cardiac function in approximately 150 patients, including normals, persons with documented coronary artery disease (CAD) persons undergoing drug therapy optimization, and one case of restrictive pericarditis. Handgrip stress was found to be a much better predictor of CAD than either rest or bicycle stress, and probe data agreed very well with ventriculography in predicting ejection fraction and other parameters in inotrophy. Because of the low radiation dose to the patient probe radiocardiography should soon find a complementary role in nuclear medicine for measurement of left ventricular reserve and for therapeutic drug intervention monitoring. Several publications and presentations have been submitted or accepted as shown in that section of this report. To provide further details one of the submitted manuscripts is excerpted below:

After giving informed consent, twenty-two patients undergoing diagnostic cardiac catheterization with coronary angiography were subjected to rest and exercise probe radiocardiography utilizing a dual crystal cardiac probe. Ejection fraction was calculated from a left ventricular time-activity curve as the fractional fall in count rate corrected for background activity.

Twenty-four to forty-eight hours prior to diagnostic cardiac catheterization, Radiocardiography (RCG) was performed at rest and during stress. Patients were in the post absorptive state and had not received any medication for 12 or more hours. Technetium-99m sulfur colloid 1 - 1.5 mCi, was injected into a peripheral vein and "flushed" into the central venous circulation with 20cc normal saline and the first pass through the cardiopulmonary circulation recorded.

After recording the resting RCG, the patient underwent isometric exercise consisting of a 5 minute sustained handgrip at 25% of maximal instantaneous voluntary effort utilizing a Jamar hand dynamometer. This maneuver has been shown to consistently increase cardiac after-load. A second RCG was recorded during the final 15 secs of hand grip.

After allowing 10 minutes recovery, a third RCG was obtained to assure return of ejection fraction and pulmonary transit time to baseline levels.

Dynamic exercise was then performed in a graded fashion utilizing a table-mounted pedal-mode ergometer. Electrocardiographic monitoring was maintained throughout this period of stress. Exercise was maintained until the patient had reached 85% maximum predicted heart rate, fatigue, or angina. RCGs were obtained at a heart rate of 100 and at termination of stress.

Of 21 patients studied, two patients had isometric stress only, and four patients had dynamic stress alone. The remaining 16 patients had both procedures.

Each patient in the study had complete coronary angiography. Coronary disease was considered significant if there was 50% or greater narrowing in luminal diameter.

Angiographically normal individuals increased ejection fraction with either form of stress. Isometric stress produced no change or a fall in LVEF in all patients with coronary disease. Dynamic exercise, however, induced significant increase in LVEF in six of fifteen patients with significant coronary disease. There was considerable overlap between these six patients and the normal subjects, which precluded complete separation by bicycle ergometry. Using failure of LVEF to increase with exercise as an indicator of disease, either bicycle ergometry or sustained handgrip was able to detect disease ($p < .01$ by

chi square analysis with Yate's correction); though isometric stress was a better discriminator than dynamic exercise. In the 16 subjects undergoing both forms of stress, analysis with a Student's paired t-test confirmed that a difference existed ($p < .01$) between LVEF during isometric stress and during rhythmic exercise. It is interesting to note that even isolated narrowing of a right coronary artery was consistently associated with a fall in LVEF during isometric stress (6 patients).

Exercise electrocardiography is widely utilized in evaluating patients with possible coronary artery disease, though it suffers severe limitations in diagnostic accuracy. Myocardial perfusion imaging with Thallium-201 has demonstrated improved sensitivity and specificity, but is costly, time consuming, and is usually done in conjunction with standard treadmill electrocardiography. More recently, attention has focused on ventricular functional evaluation during exercise as a means of identifying individuals with impaired ventricular reserve as a result of coronary disease.

Based on our observations that LVEF was sensitive to drug-induced changes in cardiac afterload, the present study was designed to determine whether or not changes in LVEF during a physiologically-induced increase in afterload might be a more sensitive indicator of impaired ventricular reserve than that observed with conventional dynamic exercise.

While isometric stress might not impose significant aerobic requirements on the exercising individual hemodynamic changes which may affect cardiac performance do occur. During sustained submaximal handgrip there is an increase in mean arterial pressure, coronary sinus blood flow, and myocardial oxygen consumption, while systemic vascular resistance (SVR) either increases or remains unchanged (as opposed to the drop in peripheral resistance with dynamic exercise). This response is centrally mediated and is proportional to the relative force and duration of sustained isometric contraction. It is independent of the absolute force of contraction or the mass of muscle contracting isometrically. Large increases in SVR have been observed in subjects attempting to contract muscles in transiently paralyzed limbs. Extensive animal studies have also confirmed the role of the central nervous system. The overall effect is one of marked increase in afterload with isometric exercise in contrast to that resulting from dynamic stress.

Probe radiocardiography was chosen as the technique for measuring LVEF in this study. A cardiac probe has only recently become commercially available, thus this technique is not in widespread use. The estimated standard deviation for multiple serial LVEF determinations by this technique is .0257. Several advantages make

this technique preferable to the usual "gated" radionuclide study. The scintillation probe is much more sensitive than a gamma camera, achieving a hundred-fold increase in sensitivity (count-rate) with a ten to twenty-fold decrease in injected dose. Since it is a "first-pass" recording, it requires only 10-15 seconds per study and can measure LVEF at peak stress rather than averaging it over a period of minutes. Finally, the currently available probe requires a considerably smaller investment in purchase and maintenance than a camera-computer system.

Our data indicates that there is a significant difference in the response of the left ventricle to isometric stress compared to dynamic stress when a paired t-test was performed on the sixteen subjects undergoing both forms of exercise ($p < .01$). All normal subjects increased LVEF with either form of stress. However, the reduction in LVEF with isometric exercise in subjects with coronary disease was both greater in magnitude and more consistent in occurrence than that observed during bicycle ergometry. This confirms our early impression of the sensitivity of LVEF to afterload modification, and supports the clinical observation that isometric stress may elicit latent impaired ventricular compliance or ventricular dysfunction as manifest by the development or accentuation of abnormal apical diastolic gallop sounds.

This study has demonstrated the feasibility of using sustained hand-grip exercise in conjunction with radiocardiography to evaluate functional ventricular reserve by assessing changes in LVEF during stress. The simplicity, low morbidity, and enhanced accuracy in delineating normal and coronary disease subjects, when combined with a low-cost study, suggest a useful role for handgrip radiocardiography in screening for cardiac disease.

Summary of Data

<u>Patient</u>	<u>Diagnosis*</u>	<u>Treadmill ECG**</u>	<u>Left Ventricular Ejection Fraction</u>	<u>Handgrip</u>	<u>Bicycle</u>
MV	RLC	I	58	-	51
SN	N	N	76	-	90
BT	N	N	77	-	96
OG	N	P	81	-	87
HC	RL	P	64	64	63
JB	RL	P	81	81	95
AT	RLC	I	81	62	66
VA	R	N	75	64	80
RM	RLC	I	36	36	40
EL	R	P	85	62	79
WG	N	N	71	77	82
JH	RLC	P	54	48	65
CS	R	P	80	71	72
HR	N	N	70	77	80
WR	N	N	65	79	88
BV	R	P	85	71	81
CT	N	I	60	63	76
EM	R	P	67	59	76
AW	RLC	P	86	69	67
PH	RLC	P	65	54	-
GR	RLC	P	84	82	-
FR	R	N	65	52	83

*Vessels with 50% or greater narrowing of luminal diameter.

R = right coronary artery,

L = left anterior descending coronary artery,

C = circumflex coronary artery,

N = no significant coronary obstruction

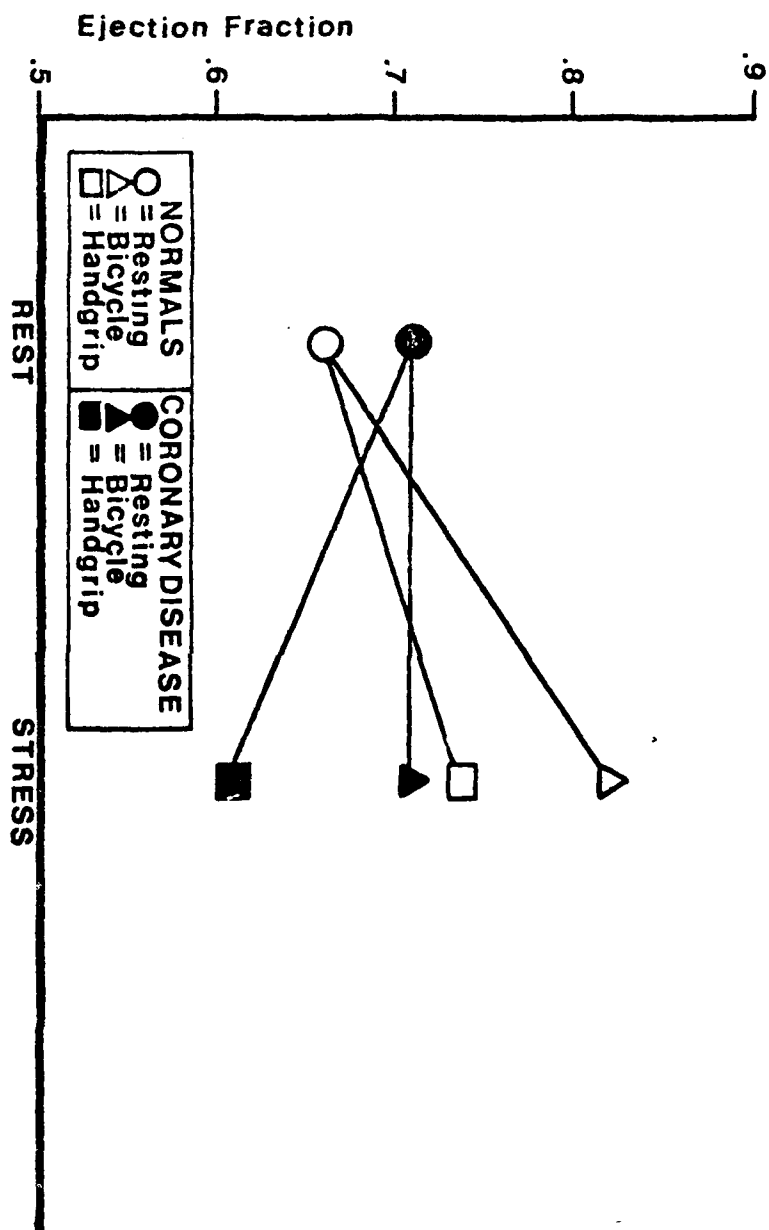
** P = positive test, ST depression 1 mm;

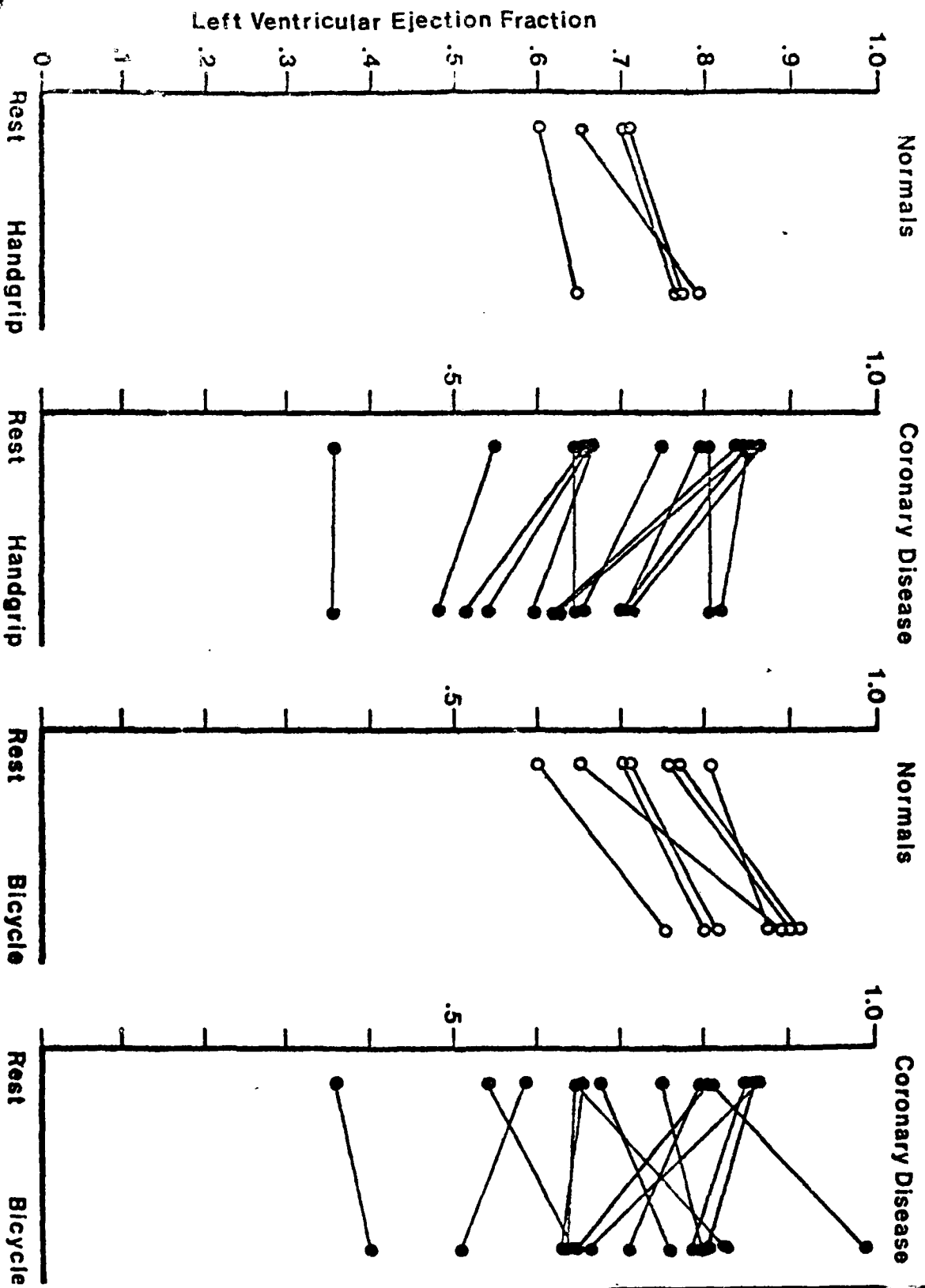
N = negative test,

I = indeterminate, abnormal but nondiagnostic

Diagnostic Parameters for Treadmill ECG and Stress Radiocardiography

	<u>Treadmill ECG</u>	<u>Handgrip RCG</u>	<u>Bicycle RCG</u>
Sensitivity	60%	100%	60%
Specificity	45%	100%	100%
Negative Predictive Value	54%	100%	40%
Positive Predictive Value	91%	100%	100%
Accuracy	73%	100%	72%
	r = 22	n = 18	n = 20
	N.S.	p < .001	p < .01





CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Effect of Catecholamines and Antagonists on Insulin Dependent
Glucose Uptake by the Bladder of Bufo Marinus

WORK UNIT NO: 77/27

PRINCIPAL INVESTIGATOR MAJ Gerald Kidd, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the mechanism of action of insulin on glucose transport across the toad bladder.

TECHNICAL APPROACH

The toad bladder epithelium appears to be an analog of the distal tubule collecting duct complex of the mammalian kidney. The effects of alpha and beta adrenergic blocking drugs on glucose transport in this system will be studied.

PROGRESS

The principal investigator on this study has been reassigned. No progress was reported.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Effect of Temperature of the Test Meal on Gastric Emptying Time

WORK UNIT NO: 78/02

PRINCIPAL INVESTIGATOR MAJ J Floyd MD, MAJ C. M. Lund, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effect of temperature of a test meal of 500cc saline on the gastric emptying time (GET) of that meal.

TECHNICAL APPROACH

The patient population for this study will be volunteers obtained through the Gastroenterology Clinic. Ten (10) normal subjects will be studied. Patients who are under 18, pregnant, or lactating will not be done. Studies on women of child bearing age will be done during the first ten (10) days following the onset of menses. Gastric emptying will be measured by the method of Chaudhuri utilizing Tc-99m DTPA. GET will be measured three times in each subject; in each case the saline/Tc-99m DTPA will vary from "cold" (4°C) to "warm" (24°C), to "hot" (42°C). The test will be done on three consecutive mornings following an overnight fast. The order in which the temperature varies will be randomized.

PROGRESS

Both investigators resigned from the Army. No progress was reported.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Comparison of Cellular Metabolic Indices with Thyroid
Dysfunction and Therapy

WORK UNIT NO: 78/06

PRINCIPAL INVESTIGATOR MAJ M. E. Sellers, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To clarify the relationship and clinical usefulness of systolic time intervals as an index of cardiac output and myocardial contractility, O_2 consumption at rest and at steady state exercise, 2,3-diphosphoglycerate (2,3-DPG), measurements in hyperthyroid, euthyroid and hypothyroid patients and to evaluate the possible use of these parameters in monitoring therapeutic interventions.

TECHNICAL APPROACH

Prior to initiation of therapy, hypothyroid and hyperthyroid patients will be screened for factors influencing 2,3-DPG levels. The patients will then undergo testing of hematocrit, hemoglobin, 2,3-DPG, pO_2 , PCO_2 , pH, bicarbonate, serum CO_2 , O_2 consumption at rest and exercise steady state, and systolic time intervals at rest. Hyperthyroid patients will be tested prior to therapy, after one week of propranolol therapy, and at time of achieving a clinical and thyroid function euthyroid state by means of I131 therapy and/or propylthiouracil or methimazole. Hypothyroid patients will be tested prior to therapy and at time of achieving a clinical and thyroid function euthyroid state by means of levothyroxine therapy. Euthyroid goiter/nodule patients will be tested prior to therapy and at a therapeutic steady state approximately 2 months after initiation of suppression therapy with levothyroxine. Factor analysis will be applied to clinical indices, thyroid function tests, 2,3-DPG, systolic time intervals and resting and exercise steady state O_2 consumption with correlations being made to thyroid dysfunction state and therapeutic measures utilized.

PROGRESS

The principal investigator has resigned, and MAJ Sellers of the Clinical Investigations Service is managing the data. The CIS is attempting to interest ~~rest~~ newly assigned staff in completing this protocol.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Minoxidil as an Anti-hypertensive in Patients Refractory to
Available Medications

WORK UNIT NO: 78/13

PRINCIPAL INVESTIGATOR CPT L. M. Lehmer, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The objective of this protocol is to test the hypothesis that minoxidil is an effective alternative treatment for patients whose blood pressure is refractory to available drugs or who have experienced unacceptable side effects from them and whose situation is life-threatening. Another purpose is to document clinical experience with minoxidil in a manner that will provide a basis for extrapolation of the results to the specified hypertensive population.

TECHNICAL APPROACH

Patients with severe hypertension, unresponsive to conventional medication and in a life threatening situation will be placed on a regimen of Minoxidil. The ultimate purpose is to control refractory blood pressure problems such as sustained severe, accelerating, or malignant hypertension. Very thorough recordkeeping will be maintained documenting unresponsiveness to conventional treatment and responsiveness to Minoxidil.

PROGRESS

The annual review of this protocol was conducted by the WBAMC Human Use Institutional Review Committee 26 Jul 79. At that time three patients had been entered. Hypertension was under control and no complications had been recognized.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

Evaluation of a Simple Device for Measuring Pulmonary
TITLE: Transit Time and its Value as a Predictor of Congestive
Heart Failure in Acute Myocardial Infarction

WORK UNIT NO: 78/18

PRINCIPAL INVESTIGATOR MAJ D. Albers, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this study is to assess the clinical utility of a simple device for measuring pulmonary transit time in patients with acute myocardial infarction.

TECHNICAL APPROACH

All patients admitted to the Coronary Care Unit at William Beaumont Army Medical Center, with a diagnosis of possible acute myocardial infarction will be entered into the study. Two hundred patients with myocardial infarct will be studied. A radiation detector will be positioned over the heart as determined by clinical examination. The radiopharmaceutical will be injected intravenously through an arm vein or through a pre-existing catheter if already in place. The radiopharmaceutical will be "flushed" into the central circulation with 20cc normal saline. The cardiopulmonary transit during the first pass through the heart and lungs will be monitored and recorded by an instrument. The radiopharmaceutical agent for this projection will be Tc-99m pertechnetate, a radiopharmaceutical approved for vascular flow studies. The dose will be 3-600uCi, a dose far less than utilized for any other routine procedure with this agent. Anticipated number of persons to be studied is approximately 60 per month, of which approximately 15 will represent true myocardial infarction. Periodic evaluation of results will be made in six month intervals to evaluate utility of information in terms of patient care, physician knowledge, and medical training.

PROGRESS

The principal investigator withdrew the protocol and has resigned from the Army.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Evaluation of Exercise Ejection Phase Indices in the Diagnosis
of Coronary Artery Disease

WORK UNIT NO: 78/19

PRINCIPAL INVESTIGATOR MAJ D. Albers, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this study is to evaluate the diagnostic accuracy, sensitivity, and specificity, of changes in systolic ejection rate with hand grip stress as measured by radionuclide techniques when applied to patients with coronary artery disease.

TECHNICAL APPROACH

Patients undergoing routine coronary angiography for established indications will be studied. Written consent will be obtained. Left ventricular ejection fractions and systolic ejection rates will be obtained at rest and during the termination of the period of isometric handgrip exercise. The patients will be injected with 20 mCi of Tc-Human Serum or an approved radiopharmaceutical for cardiac imaging. Ejection Fraction and systolic ejection rates will be measured at rest and during stress in a modified 45° LAO projection period. In addition a resting study will be obtained in a 30° RAO projection for completion of the study and maximum information yield to the attending physician. Data will be processed with a dedicated nuclear medicine computer planned for acquisition. Approximately twelve patients will be studied monthly.

PROGRESS

None

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Comparison of Left and Right Ventricular Function Response
to Stress in Patients with Coronary Artery Disease

WORK UNIT NO: 78/20

PRINCIPAL INVESTIGATOR MAJ D. Albers, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The goal of this study is to establish the functional reserve of the right ventricle in patients with coronary artery disease and normals, and to investigate the association of right coronary artery disease and right ventricular dysfunction.

TECHNICAL APPROACH

Patients will be limited to those having recently undergone coronary artery catheterization for established indications. A minimum of five and a maximum of ten patients with no demonstrable coronary artery obstructions will be evaluated in order to establish normal controls. Thirty patients with varying degrees of coronary artery disease will be entered into this study. The patients will be injected with 20 mCi Tc-99m human serum albumin (an approved radiopharmaceutical for cardiac imaging). The patients will be imaged in a supine position with the gamma camera detector head positioned in a modified 45° LAO projection. Data acquisition will require approximately two minutes for reliable determination of biventricular ejection fraction by a dedicated nuclear medicine computer. Patients will be required to sustain a handgrip of 25% maximum voluntary contraction using a JAMAR hand dynamometer for a period of six minutes. During the final two minutes, a second acquisition of data would be performed and processed for measurement of stress ejection fraction. Results at rest and stress right and left ventricular ejection fractions would be related to findings by contrast angiography. Radiopharmaceuticals will not be administered to pregnant or lactating females or persons under 18 years of age. Approximately 15 persons will be studied per month.

PROGRESS

None

STATUS: Principal investigator resigned from the Army. Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Separation and identification of CPK Isoenzymes by
Radioimmunoassay Technique

WORK UNIT NO: 78/31

PRINCIPAL INVESTIGATOR: Herbert W. Henry, MAJ, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this study is to develop a routine method for measuring CPK isoenzyme levels with emphasis on the MB fraction using RIA techniques.

TECHNICAL APPROACH

Individual isoenzymes of CPK obtained from commercial sources will be injected into rabbits to elicit specific antibody responses. The analysis for CPK would be performed by classical RIA techniques. CPK would be tagged and reacted in varying concentrations with the individual antibodies produced and harvested from the rabbits. Standard concentration curves and cross-reactivities would be established to determine RIA specificity. From the standard curves, unknown CPK concentrations in serum will be determined. It would then be possible to correlate values for the MB fraction in the normal and infarcted populations.

PROGRESS

This is a new study which has not yet commenced. The original principal investigator resigned. The new principal investigator assumed the protocol in September 1979.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEALMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Measurement of Pulmonary Function During Laparoscopy

WORK UNIT NO: 79/02

PRINCIPAL INVESTIGATOR: MAJ David K. Fenner, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The data obtained from the three sets of forced vital capacities will be analyzed with respect to the change in FVC, FEV₁, FIV₁%, and MTF occurring during the performance of laparoscopy. This analysis will be performed by the Pulmonary Department. Our purpose is to determine whether the distension of the abdomen with N₂O causes significant compromise in patients' airflow or lung volume. We expect to see a restrictive defect, but the data will be of benefit even if no changes are documented. This is important clinically since patients with chronic lung disease could have significant morbidity and/or mortality if there is compromise of their pulmonary status during laparoscopy.

TECHNICAL APPROACH

Subjects will be patients undergoing laparoscopy performed by the gastroenterology staff and fellow at WBAAC. Immediately prior to laparoscopy, with the patient in the supine position, routine pulmonary function tests will be measured. These baseline PFT's (PFT #1) will serve as controls. Following completion of PFT #1, the preparation for laparoscopy will begin in the standard manner, including premedication, I.V. with atropine, meperidine, and hydroxyzine hydrochloride (Vistaril) intramuscularly. A second set of PFT's (PFT #2) will be recorded prior to the insufflation of nitrous oxide into the abdominal cavity. Nitrous oxide will be introduced into the abdominal cavity. When adequate abdominal distension has been obtained, the pneumoperitoneum needle will be removed and routine PFT's will again be measured (PFT #3). The remainder of the laparoscopy will then be performed.

We would anticipate that the inclusion of the three sets of spirometries will add less than five minutes to the procedure. There will be no added discomfort or morbidity to the patient from these noninvasive procedures. The need for laparoscopy must be agreed upon by the gastroenterology staff, not to include the principal investigators. Informed consent will be obtained from all patients.

PROGRESS

The principal and associate investigators resigned from the Army.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Technetium-99m-pyridoxylidoneglutamate (Tc-99m-PG) for Diagnosis of Hepatobiliary Disease

WORK UNIT NO: 79/05

PRINCIPAL INVESTIGATOR: MAJ H.W. Henry, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the clinical efficacy of Tc-99m-PG as a diagnostic hepatobiliary and gallbladder agent. TC-99m-PG is presently being evaluated for its ability to provide clinically useful information regarding biliary tract and gallbladder disease processes [1-3]. This radionuclide has already been shown to be valuable in the assessment of hepatobiliary function, diagnosis of acute cholecystitis, evaluation of gallbladder dysfunction, and in differentiation of hepatocellular disease from extra-hepatic obstructive jaundice.

This additional diagnostic agent could provide more rapid diagnoses in diseases of the biliary tract and gallbladder than with the standard methods presently available. Earlier diagnoses of abnormalities could decrease patient suffering overall and particularly in the acutely ill.

Tc-99m-PG has been demonstrated to have a wide margin of safety, thereby avoiding the risk of reactions. A high incidence of reactions, including fatal reactions, is known to occur with intravenous cholangiographic contrast materials utilized in conventional radiography. The actual incidence of reactions to intravenously administered cholangiographic contrast media overall is not accurately established since no consistent efforts have been made to report nonfatal reactions. The incidence of fatal reactions following intravenous cholangiography is approximately 0.0025% or 1:40,000. Because of the rapid blood clearance of Tc-99m-PG more rapid diagnoses may be made in acute cholecystitis (i.e., within one hour), whereas, conventional radiographic methods may require several hours. Quantitative assessment of hepatobiliary function is possible with Tc-99m-PG. Tc-99m-PG may allow improvised visualization of the biliary system, even when the serum bilirubin level is mildly elevated.

Lack of B - radiation allows the use of doses up to 15 mCi giving statistically more valuable information about biliary function than with I-131-rose bengal.

TECHNICAL APPROACH

The patient population for the study will consist of active duty, retired, and appropriate dependent personnel who have suspected acute or chronic hepatobiliary disease processes.

Patients who are pregnant, lactating or who are under the age of 18 years will not be studied unless the indications for the study and the benefit to be gained outweigh the potential risk to the patient. Female patients of childbearing age will be studied within approximately 10 days following the onset of menses. Patients after 10 days menses will be evaluated for benefit versus risk. A series of patients who fulfill the above criteria will be injected intravenously with Tc-99m-PG. The adult dose will consist of approximately 15 mCi. For patients under 18 years of age that dose will be calculated according to the weight or approximate body surface area of the patient. Each patient study will be carried out under the supervision of a physician. The instruments used for detection will be the gamma scintillation cameras located at the William Beaumont Army Medical Center, Nuclear Medicine Service.

Each patient will be studied following a 4-6 hour period of fasting when possible. Following intravenous administration of the Tc-99m-PG sequential scintiphotos will be obtained at 5 minute intervals for up to one hour following injection. Simultaneous computer acquisition of the data will be obtained for further analysis. Nuclear images will be made and stored on film and/or on magnetic tape or data storage disks. Curve plot data can be subsequently derived from this information when appropriate.

In selected patients who have suspected chronic gallbladder disease, delayed images may be obtained at 2-4 hours post-injection when deemed necessary. If gallbladder dysfunction is suspected in patients who have chronic symptoms but who have been shown not to have calculi by routine oral cholecystography evaluation of gallbladder emptying may be obtained by intravenous injection of Kinevac (Sincalide for injection - manufactured by E.R. Squibb & Son, Inc. and currently used in routine oral cholecystography). The dose recommended by the manufacturer is 0.02 mcg. per kg. This methodology offers the advantage of a standardized, precise and reproducible quantitative assessment of gallbladder contractibility (better than oral fatty meals etc., used in conventional radiographic techniques in the past). This will allow computer analysis and printout of data for determination of a washout curve as gallbladder emptying occurs. Prescription forms, patient charts, and consultation forms will be used to record pertinent data.

PROGRESS

Approval from OTSG was received 24 Jul 79. No patients were entered in FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Effect of Isoniazide (INH) On Prolactin and Gonadal
Function

WORK UNIT NO: 79/06

PRINCIPAL INVESTIGATOR: MAJ G. Kidd, M.D.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Pyridoxine may be an important cofactor in the tonic inhibition of prolactin secretion. INH can cause pyridoxine deficiency and elevated prolactin levels. Prolactin effects gonadal function and we propose to study these processes.

TECHNICAL APPROACH

Complete prolactin and gonadal evaluation in patients before and during initial treatment.

PROGRESS

The principal investigator is being transferred, therefore the study will be continued at Fitzsimons Army Medical Center.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Incidence of HL-A B27 Positivity in "Idiopathic" Aortic Insufficiency

WORK UNIT NO: 79/13

PRINCIPAL INVESTIGATOR: CPT B. Lynn Feaster, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if "idiopathic" aortic insufficiency can be an isolated manifestation of the spectrum of HL-A B27 associated syndromes.

TECHNICAL APPROACH

Aortic insufficiency has been associated with ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, Reiter's syndrome and incomplete Reiter's syndrome. It occurs in 1-4% of patients with ankylosing spondylitis. The various manifestations of these syndromes present asynchronously, some occurring years before the complete syndrome and others years later. With incomplete Reiter's Syndrome arthritis is the major manifestation to occur. There is a high association between HLA B27 tissue type and ankylosing spondylitis, psoriatic arthritis, ulcerative colitis, Reiter's Syndrome, and post-dysenteric arthritis. With the known variation in presentation of the different aspects of the disease, it is possible that isolated events occur without development of any other manifestation. It has been shown that anterior uveitis, which is frequently associated with these diseases, can present without arthritic pathology. There is an increased HLA B27 antigen associated.

The purpose of this study is to try to identify a genetic subgroup among people with isolated aortic insufficiency who represent a single manifestation of the HL-A B27 positive spectrum of disease. Charts of patients with AI from the Cardiology and Internal Medicine Clinics of this hospital will be reviewed to rule out a history of Rheumatic Fever, Syphilitic aortitis, SBE, and for presence of an arthritis history. Physical examination will be used to confirm univalvular disease and absence of Marfan's syndrome. Those patients that fit the criteria will have HL-A tissue typing performed which requires one vial of blood. Appropriate x-rays will be taken when history and physical examination indicate.

At least 30 to 50 patients will be needed in the study to have meaningful results. It should take from nine months to one year to accumulate the patients and laboratory data. Controls will consist of people with acute insufficiency with definite etiology.

PROGRESS

This study was not approved by HSC until FY80 (10 Oct 79)

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Clearing of Bacteria from Sputum of Patients with Chronic Bronchitis
or Pneumonia Following Antibiotic Therapy

WORK UNIT NO: 79/14

PRINCIPAL INVESTIGATOR: CPT B.L. Feaster, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The objective of this study is to determine the amount of time required for sputum from patients with chronic bronchitis and or pneumonia to become clear after antibiotic therapy is initiated.

TECHNICAL APPROACH

The rate of clearing of bacteria from urine and blood following antibiotic therapy has been described. In respiratory disease the rate of clearing of clinical symptoms and radiographic abnormalities is known. However, the rate of clearing of bacteria from sputum in patients with infected airways or pneumonia is not known. The purpose of this study is to determine that rate of clearing. Correlation with clinical status and response to therapy will be analyzed.

Patients admitted to the medical services of William Beaumont Army Medical Center with chronic bronchitis or pneumonia will have a sputum collected for gram stain and culture on admission. After appropriate antibiotics have been begun, subsequent sputum samples will be collected for gram stain at 6, 12, 24 and 48 hours after admission and the presence or absence and type of bacteria present will be noted.

Patients admitted with the above diagnoses will be used regardless of age and sex. Thirty to fifty patients will be used. No controls will be included. The approximate time to completion will be about six months.

PROGRESS

The study was not approved by HSC until FY80 (1 Oct 79)

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7410: Chronic Lymphocyte Leukemia Protocol

WORK UNIT NO: 79/15

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the response rate, both complete and partial, in chronic lymphocytic leukemia, to combination chemotherapy with: a) Cyclophosphamide, adriamycin and prednisone (CAP) as primary therapy in patients who have had no prior chemotherapy. b) CAP as secondary therapy for those patients who have previously received low dose chlorambucil. To assess the effectiveness of intermittent cyclophosphamide and prednisone in maintaining a remission.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7433: Stage I & II Non-Hodgkins Lymphoma

WORK UNIT NO: 79/16

PRINCIPAL INVESTIGATOR: MAJ P. C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, I_E, II_E treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone, with extended field radiotherapy plus combination chemotherapy (CHOP).

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7436: Combined Modality Therapy of Breast Cancer

WORK UNIT NO: 79/17

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrence in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7440: Adjuvant Chemotherapy for Osteogenic Carcinoma

WORK UNIT NO: 79/18

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of combination chemotherapy with CY-VA-DIC (cyclophosphamide, vincristine, adriamycin and DIC) in preventing the development of metastases in patients with osteogenic sarcoma who have received definitive surgery for their primary lesions and who have no evidence of residual disease. To determine the survival and disease-free interval pattern of patients on this study to be compared to historic controls in the medical literature.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7410: Adjuvant Chemotherapy for Patients with
Locally Advanced Adenocarcinoma of the Large Bowel

WORK UNIT NO: 79/19

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeDNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Guerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by LTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7518: Stage IIIA and B Hodgkins Disease Remission Induction
TITLE:by Radiation Therapy Plus Chemotherapy Combination Versus Chemo-
therapy Alone.

WORK UNIT NO: 79/20

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the effectiveness of 10 courses of a 5-drug combination chemotherapy (including nitrogen mustard, vincristine, procarbazine, prednisone, and bleomycin) program against the combined 3 courses of chemotherapy followed by total nodal irradiation therapy program for complete remission induction in patients with Stage III asymptomatic A or symptomatic-B Hodgkin's Disease.

To evaluate the systematic "restaging" of patients in apparent complete remission.

To assess the length of unmaintained remission after intensive induction with 10 courses of chemotherapy treatment versus the combination chemo-radiation therapy, after documentation of CR status by careful "restaging."

To assess the toxicity of the chemotherapy alone portion of the study versus the toxicity of the combination of chemotherapy and radiation therapy.

To intercompare the results of this program with those to be obtained by the ongoing MOPP #5 study (SWOG-7406).

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7521: Adjuvant Melanoma

WORK UNIT NO: 79/21

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of BCNU, hydroxyurea, and imidazol carboxamide (RIM) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence.

To determine the efficacy of combination chemotherapy (BHD) with and without BCC in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised (Minimal residual disease)

To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis.

To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by LTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Combination Chemotherapy for Advanced Soft Tissue Sarcomas

WORK UNIT NO: 79/22

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the maximal effective chemotherapy induction regimen for patients with disseminated soft tissue sarcomas who have probability of response >50%. To determine if cycling the use of adriamycin and maintenance with CY-DIC-DACT increases the duration of CR's treated initially with A-DIC.

TECHNICAL APPROACH

The details are lengthy and specified in the original S^{OG} protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7630: Chemotherapy of Advanced Prostatic Cancer

WORK UNIT NO: 79/23

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the rate or response of hydroxyurea to a two-drug combination of adriamycin and cyclophosphamide in patients with advanced carcinoma of the prostate who have measureable disease (Stage D-bone metastases or extrapelvic disease).

To compare the duration of survival in patients with no measureable disease treated with one of the treatment regimens.

To estimate the response rate to each crossover regimen in patients that have been treated and did not respond to one of the regimens.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by LTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7632: Combined Modality for Recurrent Breast Cancer

WORK UNIT NO: 79/24

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal chemotherapeutic approach.

Determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.

Correlate hormonal manipulations with estrogen and progesterone receptors where possible.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7632: Combined Modality for Limited Squamous Carcinoma of Lung

WORK UNIT NO: 79/25

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether chemotherapy with adriamycin and/or immunotherapy with levamisole, improve median survival of split-course radiotherapy used alone in the treatment of patients with limited extent, squamous bronchogenic carcinoma.

To determine the qualitative and quantitative toxicity of each treatment regimen.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO TEXAS 79920

DETAIL SHEET

TITLE: SEOG 7703: Treatment in Combination with BCNU, DTIC, or
Procarbazine in Patients with Malignant Gliomas of the Brain

WORK UNIT NO: 79/26

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this study is to compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus Procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

TECHNICAL APPROACH

The details are lengthy and specified in the original SEOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAHC, and are available upon request.

PROGRESS

This is a new study at WBAHC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7704/05: Chemoinmunotherapy for Multiple Myeloma VMCP +
TITLE: VSMCP.VBAP vs MP for Induction Therapy: VMCP vs VMCP + Levamisole
for Maintenance

WORK UNIT NO: 79/27

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the effectiveness of three intermittent pulse chemotherapy combinations VMCP + VCAP vs VMCP + VBAP vs MP for induction of remissions in previously untreated patients with multiple myeloma. Results will also be compared with other combination chemotherapy treatments in previous SWOG studies, especially VMCP treatment in SWOG 7418 and previous studies of MP combinations.

For patients proven to have at least a 75% tumor regression after induction, to compare the value of 12 months of chemoinmunotherapy maintenance VMCP + Levamisole in comparison to VMCP alone.

To establish baseline and serial data on immunologic status in these patient groups.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAHC and are available upon request.

PROGRESS

This is a new study at WBAHC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7713: Chemotherapy in Non-Hodgkins Lymphoma (CHOP vs CHSO +
Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy

WORK UNIT NO: 79/28

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the effectiveness, in terms of rate of response two chemo-immunotherapy regimens (CHOP + Levamisole vs CHOP - Levamisole BCG) against CHOP for remission induction in previous untreated patients with non-Hodgkin's lymphoma

For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with Levamisole vs no maintenance therapy.

For patients with impaired cardiac function (not eligible for treatment with Adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-Levamisole-BCG, to estimate the complete response obtained by continued chemioimmunotherapy with CHOP - Levamisole.

To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.

To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.

To establish baseline and serial data on immunologic statute in both chemioimmunotherapy groups.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by OHSU prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SF00 7717: Diagnostic Studies for Patients with Adenocarcinoma
TITLE of Unknown Origin

WORK UNIT NO: 79/29

PRINCIPAL INVESTIGATOR: MAJ P.C. Early, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the yield of various diagnostic procedures in finding the site of tumor origin in patients who present with metastatic adenocarcinoma with no obvious primary source.

To compare the efficiency of combination chemotherapy using Fluorouracil, Adriamycin and Cytosin vs. Fluorouracil alone the palliative management of patients with metastatic adenocarcinoma of unknown origin.

To assess the hematologic toxicity of the chemotherapy regimen on treated patients.

TECHNICAL APPROACH

The details are lengthy and specified in the original SF00 protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7725: Continuous 5-Drug Induction with Intermittent CMF vs
TITLE: CMF + Levamisole for Maintenance in Patients with Estrogen
Receptor Negative Breast Cancer

WORK UNIT NO: 79/50

PRINCIPAL INVESTIGATOR:

MAJ D. C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the respective effects of Levamisole on the duration of response and survival of patients with advanced breast cancer concurrently treated with maintenance chemotherapy after a successful remission induction trial of continuous Cooper regimen.

To accumulate data on immunologic variables under the conditions of chemotherapy alone and combined chemotherapy and immunotherapy with Levamisole of advanced breast cancer.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAAC, and are available upon request.

PROGRESS

This is a new study at WBAAC which was not approved by PSC prior to the end of 1979.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7727/28: Skin Test Procedures for SWOG 7727/7728

WORK UNIT NO: 79/31

PRINCIPAL INVESTIGATOR: MAJ P C Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine remission induction rates, remission duration, survival and toxicity in patients with disseminated malignant melanoma treated with BCNU, hydroxyurea and DTIC(BID), plus Levamisole, and intermittent single high dose DTIC plus Actinomycin D in a prospective, randomized clinical study.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAWC, and are available upon request.

PROGRESS

This is a new study at WBAWC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7738: Combination Chemotherapy of Pancreatic Adenocarcinoma
TITLE: with Mitomycin C, 5-FU, and Streptozotocin, Phase III

WORK UNIT NO: 79/32

PRINCIPAL INVESTIGATOR: MAJ P C Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the response of pancreatic adenocarcinoma to either 5-fluorouracil and mitomycin C with or without streptozotocin.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.'

PROGRESS

This is a new study at WBAMC which was not approved by OTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7802: Adjuvant Therapy of Soft Tissue Sarcoma With
TITLE: Radiation Therapy and Chemotherapy

WORK UNIT NO: 79/33

PRINCIPAL INVESTIGATOR MAJ P C Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine whether combination chemotherapy with A-DIC can improve the results in terms of disease-free survival produced by adjuvant radiotherapy in patients with soft tissue sarcomas Stage IIB and III at high risk for recurrent disease.

To determine any difference in toxicity between patients receiving boost radiation therapy to the scar with Cobalt 60 or electron beam.

To determine any difference in local recurrence rate or disease-free survival between patients with adequate surgery and those without adequate surgery.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7804: Adjuvant Chemotherapy with 5-FU, Adriamycin and
TITLE: Mitomycin C (FAM) vs Surgery Alone for Patients with Locally
Advanced Gastric Adenocarcinoma Phase III

WORK UNIT NO: 79/34

PRINCIPAL INVESTIGATOR: MAJ P C Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy of adjuvant chemotherapy with 5-Fluorouracil, Adriamycin and Mitomycin-C (FAM) on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II AND III gastric adenocarcinoma compared to potentially curative surgery alone.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7811: Brain Metastases Phase III

WORK UNIT NO: 79/35

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the effectiveness of combined radiation therapy and metronidazole (Flagyl) in the treatment of patients with brain metastases from primary malignancies outside the central nervous system, compared with radiation therapy alone, as determined by objective response (brain and/or CAT scan) and/or increase in functional neurologic level and duration of response.

To determine the toxicity of multiple dose administration of metronidazole and radiation therapy.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by OTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7823/24/25/26: ROAP-ADOAP in Acute Leukemia, Phase III

WORK UNIT NO: 79/36

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP (Rubidazone, vincristine, arabinosyl cytosine, and prednisone) to ADOAP (the same combination using Adriamycin in place of Rubidazone) in adult acute leukemia, as determined by remission rate, remission duration and survival.

To determine the comparative toxicity of these regimens.

To determine whether late intensification therapy at 9 months after complete remission will improve longterm, disease-free survival.

To determine whether immunotherapy using levamisole for 6 months after 12 months of complete remission on chemotherapy improves disease-free survival.

To determine reproducibility of the FAB/histologic classification and correlation to response to therapy in 200 consecutive cases of acute leukemia.

To study the effects of intensive supportive care in the management of acute leukemia.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request

PROGRESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

SWOG 7828: Combined Modality Therapy for Extensive Small-Cell
TITLE: Carcinoma of the Lung. Phase III.

WORK UNIT NO: 79/37

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To improve the complete response rate and long-term disease-free survival of patients with extensive small-cell carcinoma of the lung.

To define, qualitate and quantify the toxicity of each regimen employed.

To compare the efficacy of two non-cross resistant regimens (cell-cycle specific vs. cell-cycle-nonspecific) during induction.

To determine whether administration of a second, non-cross-resistant regimen in consolidation can convert stable disease or partial response to a better quality of response.

To determine the effect of intentional, early alternation of non-cross-resistant regimens on the complete response rate.

To determine whether "reinduction" at 24 and 52 weeks has a favorable effect on response duration and survival.

To determine whether administration of intrathecal methotrexate at "reinduction" can affect the incidence of non-brain CNS relapse.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC and are available upon request.

PROGRESS

This is a new study at WBAMC which was not approved by OTSG prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: SWOG 7835: High Dose Vincristine, Prednisone, Hydroxyurea +
Cytosine Arabinoside (HOAP) in the Blastic Phase of Chronic
WORK UNIT NO: Granulocytic Leukemia, Phase III
79/38

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate the effectiveness as determined by remission rate, of the combination of high-dose vincristine, prednisone, hydroxyurea, and cytosine arabinoside (HOAP) for remission induction in patients with the blastic phase of chronic granulocytic leukemia. High-dose vincristine is used here to indicate the administration of a dose of 2 mg/m² without limiting the total dose to 2 mg.

To compare the effectiveness of this regimen in myeloid versus lymphoid blastic transformation, and in patients with poor prognostic characteristics, namely hyperdiploidy and lack of terminal deoxynucleotidyl transferase (TdT).

To evaluate the value as determined by median duration of remission and survival, of an intensive intermittent regimen of cytosine arabinoside, prednisone, and vincristine in the maintenance of remission.

TECHNICAL APPROACH

The details are lengthy and specified in the original SWOG protocol. Duplicates are kept on file in the Clinical Investigations Service, WBAMC, and are available upon request.

PROCESS

This is a new study at WBAMC which was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

STUDY C100-7005/7006: Study for Prior MOPP Failures Without Prior Anthracycline

WORK UNIT NO: 70/59

PRINCIPAL INVESTIGATOR: MAJ P.C. Farley, MD

ASSOCIATE INVESTIGATOR:

OBJECTIVES

To evaluate the effectiveness, as determined by response rate, of the ABOP combination of chemotherapy for remission induction in patients with advanced (Stages III or IV) Hodgkin's disease who have not had prior chemotherapy and in those with prior MOPP (no anthracyclines).

To assess the length of unmaintained remissions after intensive induction with ten courses of treatment with ABOP and after documentation of CR by restaging.

To evaluate the degree of noncross resistance of ABOP to MOPP failures in terms of remission induction, duration of remission and survival.

To compare the toxicities and side effects of the ABOP regimen to those of MOPP.

LITERATURE REFERENCES

No data have been directly and specifically in the original C100 protocol. Anticancer agent list on file in the Clinical Investigations Service, WAMC, and are available upon request.

REMARKS

This protocol, which at WAMC would not be approved by IRB prior to the onset of 1980.

ALL INFORMATION CONTAINED HEREIN IS UNCLASSIFIED

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEARMONT ARMY MEDICAL CENTER
FORT DAVID, TEXAS 79920

DETAILS SUBJECT

SEOC 5444: A Comparison of Methotrexate and Cis-Platinum
TITLE: for Patients with Advanced Squamous Cell Carcinoma of the
Head and Neck

WORK UNIT NO: 79/40

PRINCIPAL INVESTIGATOR: MAJ P.C. Carley, MD

ASSOCIATE INVESTIGATOR:

OBJECTIVES

The objectives of this study are to determine whether cis-platinum will give a superior response rate and/or a longer remission duration than methotrexate in patients with squamous cell carcinoma of the head and neck region.

TECHNICAL APPROACH

The details are lengthy and specified in the original SEOC protocol. Duplicates are kept on file in the Clinical Investigations Service, WBMC, and are available upon request.

PROGRESS

This is a new study at WBMC which was not approved by IRB prior to the end of FY79.

STATUS: Active

4. 2000

DETAILED SUMMARY

10. J. H. W. Lam, *Pharmazie*, **46**, 105 (1991).

1. *Chlorophyll a* and *Chlorophyll b* were determined by the method of Lichtenthaler and Whistler (1973). The *Chlorophyll a* and *Chlorophyll b* contents were expressed as $\mu\text{g g}^{-1}$ of dry weight.

DATE OF BIRTH: _____ SEX: _____

THE UNIVERSITY OF CHICAGO

ON THE THEORY OF

To determine the efficiency of high intermission doses of 20-30 mg/ml chlorazepate, 100 (N=111) 70-75% APO in patients with advanced terminal breast carcinoma refractory to higher priority treatment

to determine the nature and extent of toxicity of this agent with the goal of elucidation only of WHA-100 and minimal changes.

TECHNICAL APPENDIX

The details are lengthy and specified in the original SALL protocol. Inquiries are kept on file in the Clinical Investigations Service, NCI, and are available upon request.

1. *Journal of the American Medical Association*, 1997; 277: 1039-1043.

1. *Journal of the American Medical Association*, 1997; 277: 1033-1037.

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WILLIAM BEAUMONT ARMY MEDICAL CENTER EL PASO TX
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CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Umbilical Cord Lactate, Pyruvate, Betahydroxy Butyrate, pCO_2 , pO_2 , and pH Value in Normal and Abnormal Pregnancies

WORK UNIT NO: 74/01

PRINCIPAL INVESTIGATOR LTC W. Daniell, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the effect of labor on normal pregnancies and pregnancies complicated by placental insufficiency.

TECHNICAL APPROACH

Maternal amniotic fluid, venous, umbilical arterial and umbilical venous blood samples will be studied for the above levels. The results will be correlated with neonatal outcome and morbidity.

PROGRESS

Although this project has been suspended a prolonged time it is still considered worthwhile and will be conducted if conditions permit. The original principal investigator has retired and a new investigator has assumed the project.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

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FROM: [illegible]

SUBJECT: [illegible]

REFERENCE: [illegible]

DATE: [illegible]

CONFIDENTIAL

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CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Comparison of Clinical and Laboratory Measurements of
Gestational Age to the Actual Gestational Age as Determined
by Last Ovulation

WORK UNIT NO: 76/20

PRINCIPAL INVESTIGATOR COL David Boyce, M.D.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To test the reliability of clinical and laboratory methods of gestational age assessment by comparing the assessments to true gestational age as determined by basal body temperature curves defining last ovulation.

TECHNICAL APPROACH

Patients volunteering to record basal body temperatures prior to conception will be monitored throughout their pregnancy by serial sonography and serum estriols. The neonate will be evaluated for gestational age both in blinded and unblinded studies.

CONSUMABLE SUPPLIES

\$870

PROGRESS

Patient volunteers are too infrequent to justify continuing.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Estriol Production Rate Studies in Pregnant Women

WORK UNIT NO: 76/29

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Determination of estriol production rates in normal pregnant women and correlation in abnormal gestations with the clinical outcome.

TECHNICAL APPROACH

Estriol production rates will be estimated by the infusion of deuterated estriol into these women followed by subsequent serum sampling. A measurement of the amount of deuterioestriol present in extracted estriol samples relative to the total amount of estriol extracted would indicate the rate of endogenous estriol synthesized by the patient.

PROGRESS

Samples from one patient have been submitted to the collaborating institute, the University of Colorado, for analysis. The University cannot assist us with any patients until they receive renewal of their funding. Although several months have elapsed the protocol will be kept open in anticipation of further cooperation.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Correlation of Amniotic Fluid Cortisol and the Free Estriol Surge
in Maternal Plasma

WORK UNIT NO: 76/34

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To confirm the amniotic fluid cortisol levels at varying gestational ages. To correlate these levels with the maternal free estriol surge and the amniotic fluid L/S ratio and attempt to determine if the cortisol increase is also nonlinear and, if so, if it precedes or follows the free estriol surge.

TECHNICAL APPROACH

The amniotic fluid cortisol concentration and L/S ratios on each specimen submitted will be determined, as will plasma free estriol and cortisol when each amniocentesis is performed. The indications for amniocentesis will be based on currently accepted clinical criteria and the decision for the procedure will be made by attending and resident staff managing the patient. The analyses will be done by radioimmunoassay and TLC as presently performed in the RIA laboratories. The data will be subjected to regression analysis and appropriate rank correlation.

CONSUMABLE SUPPLIES

\$845

PROGRESS

Sixty-two study specimens were analyzed and the data presented at the Armed Forces District Meeting of the American College of Obstetrics and Gynecology in October 1977. A manuscript is in preparation regarding the 109 samples available.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Correlation of Choline Phosphotransferase Activity in Human
Amniotic Fluid and Neonatal Nasopharyngeal Aspirates

WORK UNIT NO: 76/35

PRINCIPAL INVESTIGATOR MAJ R. Heath, M.D.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To construct normograms of the activity of choline phosphotransferase in human amniotic fluid with respect to gestational age and activity of the enzyme in neonatal nasopharyngeal secretions at 6 hour intervals from birth. These levels will be related to the occurrence of idiopathic respiratory distress syndrome in the neonate. The ultimate objective is to determine whether this enzyme activity is a better predictor of idiopathic respiratory distress syndrome than the currently used lecithin/sphingomyelin ratio.

TECHNICAL APPROACH

Concurrent with otherwise medically indicated amniocentesis, 10 milliliters of amniotic fluid will be obtained and analyzed for choline phosphotransferase and phosphatidate phosphohydrolase activities. A normogram of enzyme levels with respect to gestational age will be constructed. These levels will then be correlated with the occurrence of idiopathic respiratory distress syndrome to see indeed if one or both are better predictors of the syndrome. Additionally, routine nasopharyngeal suction material will be collected at 6-hour intervals on neonates and analyzed for this enzyme activity. Levels of activity will be compared to the course of the disease in hopes of developing an objective technique for differentiating idiopathic respiratory distress syndrome from other causes of respiratory distress in the neonate.

PROGRESS

Amniotic fluid levels in uncomplicated pregnancies have been reported at the Armed Forces District of the American College Obstetrics and Gynecology meeting. Further efforts are contemplated, but a new, more inclusive protocol will be required. Data to date appeared in Pediatric Research 12:729, 1978.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Ultrastructural Investigation of Prostaglandins and Their
Precursors in the Human Fetal Chorioamniotic Membrane

WORK UNIT NO: 77/02

PRINCIPAL INVESTIGATOR LTC W. Daniell

ASSOCIATE INVESTIGATORS: B.F.F. Reiman

OBJECTIVES

To determine if prostaglandins and their precursors can be localized in fetal membrane and to detect any change with these in association with labor.

TECHNICAL APPROACH

Using indirect antibody labeling technique, prostaglandins were tagged at a cellular level. The section was then imbedded and ultra-thin sections made.

PROGRESS

Ultrathin sections have been prepared.

STATUS: Awaiting microscopic time to analyze our material.

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Inhibition of Premature Labor with Terbutaline

WORK UNIT NO: 77/04

PRINCIPAL INVESTIGATOR MAJ T. Howard, MD COL A. Killam, MD

ASSOCIATE INVESTIGATORS: LTC LL Penney, MD

OBJECTIVES

To study inhibitory effects of Terbutaline on premature labor.

TECHNICAL APPROACH

Patients with no contraindicating condition, such as ruptured BOW, intra-uterine sensis, or abruptio placenta will be treated for premature labor with either Terbutaline or a placebo. After admission to the Labor and Delivery Suite, the following procedures will be initiated:

a. Infusion of either a Terbutaline or placebo loading dose of 0.5 mg IV diluted with normal saline by the use of an infusion pump over a 50 to 60 minute interval. This loading dose may be repeated up to a maximum of 3 times per 24 hours as needed to abolish uterine activity.

b. Following the loading dose, the Terbutaline or the placebo will be given subcutaneously at a rate of 0.25 mg every 2-4 hours as needed for a 24-hour period.

c. Patients will then be maintained on oral Terbutaline, 2.5 mg every 2-4 hours, or oral placebo as previously discussed, until fetal maturity is proven or suspected or patient delivers. On-going assessment of fetal maturity will include serial ultrasound exams and may include amniocentesis for L/S ratio determination to assess fetal pulmonary maturity. Labor will be inhibited until the patient delivers or reaches a point where she is felt to represent a gestational age of 36 weeks or an estimated fetal weight of 5 pounds or demonstrates an L/S ratio of 2:1 or greater. These dosage regimens were determined from manufacturer's recommended dosage schedules and from previous studies using betamimetic agents for inhibition of labor.

PROGRESS

A submitted manuscript is excerpted below.

Effective 1 Jan 1978 all pregnant patients at this hospital whose physician prescribed terbutaline were counselled and given the opportunity to participate in the study. Patients who did not consent or who were not eligible because of arrhythmia, hyperthyroidism, hypertension or diabetes received standard treatment but terbutaline was administered only on protocol. This policy was in effect under an investigational new drug permit, but intravenous use was ordered discontinued by the FDA in July 1979. At that time 51 patients had granted informed consent.

Two patients revoked their consent before any treatment and one did so following the initial dose. Two patients were discharged on treatment, did not return to clinic, did not respond at their forwarding address, and were considered lost to followup. One patient delivered a fetus with multiple anomalies and one aborted a 259 gram fetus when infection developed post-cerclage. Of the remaining 44 candidates, five had gestational ages less than 36 weeks but delivered mature fetuses of greater than 2500 grams weight within 72 hours of admission, one had cervical dilatation greater than 4 centimeters on admission, three had abruptio placentae and two were cerclage patients. The final 33 patients comprised the study group.

Labor was diagnosed in each patient by changes in cervical dilatation or effacement and accompanying uterine contractions with a frequency of at least two every ten minutes detected by external monitor. The estimated gestational age from menstrual and clinical history was more than 24 but less than 36 weeks and the membranes were intact in all cases. A random number table was used to generate the treatment sequence and only the dispensing pharmacist knew the identity of the drug prescribed throughout the study period.

Intravenous loading was accomplished by 500 ug the first 50-60 minutes, or 10 ug/minute, repeated up to 3 times if necessary to abolish uterine activity. The uterine monitor tracings from ten minute segments at 10-20, 30-40, 60-70, 120-130, and 180-190 minutes respectively were used to assess contraction activity. Thereafter the drug was administered subcutaneously at a rate of 0.25 mg every 2-4 hours for 24 hours then 2.5 mg orally every 2-4 hours. Unless delivery occurred therapy was discontinued only when the patient reached an estimated fetal weight of 2500 grams or had an amniotic fluid L/S ratio of 2:1 but in no case prior to 36 weeks estimated gestational age. Maternal vital signs and fetal heart rate were recorded every 15 minutes during parenteral therapy, less often on oral treatment hospital days and weekly at clinic visits following discharge.

Statistical determinations were done on a Hewlett Packard 65 calculator and the groups were compared by Student's t test or chi square. Two-tailed probability tests were used.

Maternal characteristics of the two groups are shown in Table 1.

Pregnancy Status on Admission to Terbutaline Protocol for Premature Labor
(N = 33)

Therapy	Terbutaline (N=15)	Placebo (N=18)	Probable Difference
Weeks' gestation			
Mean	31.3	30.9	NS
SEM	0.8	0.7	
Cervical dilatation (Cm)			
Mean	1.5	1.4	NS
SEM	0.4	0.3	
Number of Patients Treated with Corticosteroids	8/15	6/18	NS

NS = Not significant

Physicians caring for the patients were asked to use their own criteria and record tachycardia as mild, moderate, or severe. No severe tachycardia or arrhythmia developed. Every patient developed a mild or moderate maternal tachycardia with percentages equivalent in the placebo and treatment groups. Two patients reported headaches which responded to conservative measures without discontinuing therapy. No other side effects were noted.

Therapy	Terbutaline (N=15)	Placebo (N=18)	Probable Difference
Baseline			
Mean	3.3	3.4	NS
SEM	0.2	0.2	
10-20 Minutes			
Mean	1.9	2.5	NS
SEM	0.3	0.3	
20-30 Minutes			
Mean	1.2	1.8	NS
SEM	0.2	0.3	
60-70 Minutes			
Mean	0.7	1.6	< .05
SEM	0.3	0.5	
120-130 Minutes			
Mean	0.5	0.5	NS
SEM	0.2	0.2	
180-190 Minutes			
Mean	0.2	0.3	NS
SEM	0.2	0.2	

Whereas 67% of the terbutaline group were no longer contracting by 60 minutes, only 21% of the placebo group had stopped. The percentages equalized during the next two periods and by three hours only two patients respectively in each group were contracting. Considering these four subjects, one of the treated patients delivered at three hours and the other at four days. The control patients delivered at seven hours and at 20 days.

Outcome of Premature Labor Treatment

Therapy	Terbutaline	Placebo	Probable Difference
<hr/>			
Pregnancy Extension (days)			
Mean	30.8	39.9	NS
SEM	5.8	4.1	
Birth Weight (gm)			
Mean	2487	2756	NS
SEM	164	165	
Median	2370	2780	
Infants with RDS/ Infants born	3/16	1/21	NS

NS = Not significant

As with several other betamimetic agents early reports describing the use of terbutaline were favorable. The doses employed in these studies occasionally, but not invariably, exceeded the 10 ug/min initial intravenous dose of the present study. Isolated case reports of maternal pulmonary edema associated with intravenous betamimetic administration have appeared and the authors are aware of a maternal mortality presenting as adult RDS following terbutaline and corticosteroid treatment. In a communication which contained no explanation the FDA ordered intravenous use of terbutaline on our investigational new drug permit discontinued effective July 1979. Accordingly, though the original design encompassed a larger sample, followup on patients entered to that point was completed and the code broken for this report.

Satisfactory diagnostic accuracy for premature labor in our patients is documented by initial maternal evaluation data statistically identical to similar studies, frequent uterine contractions recorded by external monitor, low mean and median birth weights and a high incidence of RDS and neonatal death. One death from RDS occurred in the treatment group and one from prematurity in the placebo group. No significant difference between groups was demonstrable for prolongation of gestation or birth weights. Diminished uterine activity occurred more rapidly in the treated group. Female infants outnumbered male infants by six in the treatment and four in the placebo group.

Although not statistically significant the higher incidence of RDS in the treated group appears noteworthy. Bergman diagnosed RDS in only 1/24 infants born prior to 36 weeks if their mothers received terbutaline compared to 5/17 in a group with additional pregnancy complications who did not receive terbutaline or any other betamimetic compound. This was reported as significant protection from RDS by terbutaline. No mothers were treated with corticosteroids. Comparing the subset of 44 patients described in the Material Section in this study 4/22 terbutaline treated and 2/26 placebo treated infants developed RDS. There is no significant difference between these two groups. If only infants who delivered prior to 36 weeks are considered, the incidence of RDS in the treated group of 4/12 is significantly different than the 1/24 reported by Bergman. Two of the four mothers whose infants developed RDS in the treatment group and one of two in the control group also received corticosteroids.

To our knowledge the present study is the only randomized double-blind trial of terbutaline in premature labor. The trial was discontinued by FDA directive and the data are of necessity limited due to small patient numbers. The data apparently support a reasonable doubt regarding efficacy at these dosages in the treatment of premature labor and fail to substantiate a report of a reduced incidence of RDS in the neonates of treated mothers. There were no deleterious effects in this study, but adverse reactions affecting the maternal pulmonary system may occur from intravenous terbutaline administration. One could speculate that higher doses might improve results without serious side effects, but further controlled investigation seems warranted prior to universal acceptance of terbutaline therapy for premature labor.

STATJS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Study to Determine the Ability of Amniotic Fluid to Inhibit
Growth of F. Coli

WORK UNIT NO: 77/06

PRINCIPAL INVESTIGATOR COL David Boyce, M.D.

ASSOCIATE INVESTIGATORS: MAJ M Sellers PhD, COL A. Killam, MD

OBJECTIVES

To devise an improved laboratory method for determining the inhibitory property of amniotic fluid.

TECHNICAL APPROACH

The growth and/or inhibition of a laboratory strain of E. coli in amniotic fluid as well as certain controlled media is to be monitored by a technique using C14 tagged glucose in the various culture media and monitored by the amount of 14 CO2 eluted as measured in a liquid scintillation counter. Maternal and cord blood serum zinc levels will be determined as well as the zinc and phosphate ratios of the amniotic fluid. An attempt will be made to correlate the inhibitory or noninhibitory effect of amniotic fluid on the E. coli as well as the zinc and zinc/phosphate ratios of this inhibitor effect to neonatal sepsis.

CONSUMABLE SUPPLIES

\$852

PROGRESS

A presentation of preliminary data was made at the Armed Forces District-American College Obstetrics-Gynecologists in October 1978. A submitted manuscript is excerpted below to further describe our work:

The development of amnionitis in patients with premature rupture of the membranes remains clinically unpredictable. Management of this complication of pregnancy, particularly prior to term, is controversial and largely provincial. Available epidemiological data is limited and may not apply in any given case. Rational decisions will only be possible if a predicting factor, or factors, can be subjected to some form of quantitation.

Such a factor may be the bacterial growth inhibition properties of amniotic fluid. As yet, the ability of amniotic fluid to inhibit bacterial growth has not been related to the development of amnionitis and neonatal sepsis. To determine if a relationship exists and to make the information clinically useful, we have utilized Buddemeyer's method to rapidly determine the presence or absence of bacterial growth inhibition in amniotic fluid. The method involves the measurement of $^{14}\text{CO}_2$ evolved from bacterial metabolism of ^{14}C tagged glucose in the culture medium. Our work confirms Buddemeyer's method and demonstrates its application to the determination of the growth kinetics of *E. coli* in various amniotic fluids. Pertinent features of this method are that it is rapid, inexpensive, reduces technician time, and makes possible the calculation of bacterial replication time. This report describes our preliminary observations with this technique.

The technique, as described by Buddemeyer, involves the use of a specially designed culture and metabolism chamber. The chamber (Fig 1) consists of an outer scintillation vial and an inner culture vial, a filter paper cylinder which is placed between the inner and outer vials and a cap which fits the mouth of the outer vial. The filter paper is cut to size (approximately 4 x 8.5 cm) and soaked in concentrated toluene solution of 2,5-diphenyloxazole-1,4-bis-(5-phenyloxazolyl)-benzene (PPO-POPOP) and dried in a desiccation chamber.

The prepared filter paper "fluor" is formed into a cylinder and placed inside the scintillation vial. The inner culture vial is inserted inside the filter paper cylinder. In order to facilitate the binding of evolved metabolic CO_2 to the "fluor", the filter paper is wetted with 0.5 ml 1 N NaOH by pipetting the solution circumferentially between the inner and outer vials. The inner vial is then charged with 10 μl of a solution containing 1 μCi of D- (^{14}C) glucose, 0.1 ml inoculum of an *E. coli* dilution, and 3 ml of test fluid (trypticase soy broth [TSB]), amniotic fluid [AF], or other culture media. After charging the inner culture vial and sealing the system by capping the outer scintillation vial, the vials are placed in a 37°C incubator.

Since incident light causes some activation of the filter paper "fluor", the incubator and scintillation counting system are kept in a darkened room equipped with a red light. We allow the scintillation/culture vials (metabolism chambers) to remain in this darkened environment for one hour before the first counts are made. This period allows the decay to background level of any incident light excitation which occurred during the preparation of the metabolism chambers.

The counting chamber is a 2-channel automatic sample changing Beckman model 1650 Liquid Scintillation System equipped with a modified model 55 teletypewriter. At the end of the first hour and each hour thereafter the metabolism chambers are simultaneously removed from the incubator and placed on the sample conveyor within the scintillation counting system. Each sample is counted for 0.5 minutes. When all samples

have been counted, they are returned to the incubator.

The *E. coli* used in this study are a type 06 obtained as a sub-culture from Dr. Rudolph Galask, Department of Obstetrics and Gynecology, University of Iowa, Iowa City, Iowa. Multiple dilutions ranging from 10^2 to 10^7 organisms/ml and stored as stock dilutions in a controlled refrigerator at $4^\circ - 6^\circ\text{C}$ were aliquoted as the inocula.

Amniotic fluids were obtained by amniocentesis done for iso-immunization studies, for maturity studies, at the time of C-section, for prostaglandin instillation in 2nd trimester abortion, and from intrauterine pressure catheters. A total of 23 fluids ranging from 14-40 weeks gestation were studied. The fluids were studied either immediately or placed in cold storage at $4^\circ - 6^\circ\text{C}$ and studied up to two weeks later. The fluids were neither centrifuged nor passed through a millipore filter.

As the method is extremely sensitive to environmental conditions, a control TSB culture was run on each day one or more amniotic fluids were studied. The data obtained were plotted on semi-log graph paper. Replication times were calculated using the following formula:

$$\ln A_{t_2} - \ln A_{t_1} = K(t_2 - t_1)$$
$$t_{2x} = \frac{.693}{K}$$

Where $\ln A_{t_1}$ and $\ln A_{t_2}$ are the natural logs of the sum of the scintillation counts at time t_1 and t_2 respectively, K is the slope, and t_{2x} the replication time. Since three points are needed to show linearity and since we take counts only once per hour, it is necessary that $t_2 - t_1 =$ at least 120 minutes. A detailed formula derivation has been published by Buddemeyer.

The decay of incident light excitation is shown in Fig. 2. To demonstrate this, we prepared three metabolism chambers as described, but without charging the inner culture vials. The metabolism chambers were placed in the darkened scintillation counting system and counted every three minutes. CPM were at background level within 40 minutes.

Fig 3 shows the growth curves obtained when three different concentrations of *E. coli* were inoculated into trypticase soy broth. From stock dilutions of *E. coli* containing 10^2 , 10^4 , and 10^6 organisms/ml, 0.1 ml of each dilution was added to separate culture vials containing 5 ml of TSB. These curves demonstrate the ability of this radiometric method to discriminate differences in bacterial concentrations.

Figure 4 is a composite of growth curves obtained in amniotic fluids and TSB with known and unknown amounts of growth inhibiting factors present. The bacterial inoculum for these studies was 0.1 ml of an *E. coli* dilution containing 10^4 organisms/ml. Five basic growth patterns are identified. Sections A and B represent the extremes: no inhibition (A) and complete inhibition (B). Sections C, D, and E are representative of intermediate growth patterns.

Figure 4A demonstrates a characteristic that requires explanation. Although the growth curves in TSB and AF are similar and the replication times are equal, the CPM of the AF are lower at each hour. The TSB which we use is glucose free whereas amniotic fluid is not. The ^{14}C glucose, therefore, is in competition with the nontagged glucose in the amniotic fluid. In studying TSB containing various concentrations of glucose, we have shown an inverse relationship between the CPM and the glucose concentration, but no change in the general shape of the growth curve or calculated replication times. This is demonstrated in Figure 5 where the upper curve is TSB without glucose and the lower curve is TSB containing glucose (25 mg/dl).

Section F of Figure 4 demonstrates the ability of this method to discriminate different bacterial growth curves with known concentrations of a growth inhibiting substance (ampicillin) present in the culture medium. These growth curves also demonstrate the extremes of no inhibition, complete inhibition, and intermediate patterns. Table 1 relates the calculated replication times for each of the ampicillin concentrations.

The effects of inhibitory factors in amniotic fluid or culture media are best appreciated by examination of the graphed data rather than the calculated replication times. When the scintillation counts are near background level, there will be a small variation from one counting cycle to the next giving rise to the possibility of a minimally positive slope over a given two hour period when, in fact, the slope is essentially zero and the replication times infinite. This is demonstrated in Fig. 4E and Fig. 4F (12.5 and 18.8 $\mu\text{g/ml}$ ampicillin). Fig. 4E shows what is essentially a prolonged lag phase and slow replication time. It is obvious from the graphed data that there was a period of accelerated growth, but since no counts were made between the 11th and 26th hours, the exact rate cannot be determined.

If information regarding bacterial growth inhibition by amniotic fluid is to be clinically useful, we must be able to demonstrate this inhibition in a short time period. The radiometric measurement of bacterial metabolism as described by Buddemeyer and herein adapted would appear to provide this laboratory tool.

Previously reported studies regarding amniotic fluid inhibition of bacterial growth have used plate counts or turbidity techniques to show bacterial growth. Plate count techniques require 12-24 hours of incubation. Turbidity techniques lack sensitivity and are limited by the clarity of the fluid or culture media.

Most previously reported studies also make use of inocula from fresh broth cultures, thus adding another 12-24 hours to the time needed to obtain a result. In our adaptation of the radiometric technique we made use of *E. coli* dilutions which were made up in TSB, verified by turbidity and plate counts, and stored in temperature controlled refrigerator. This provides readily available inocula of known concentrations.

Plate counts done intermittently on stored cultures showed no significant change in counts over a 75 day interval, however, there was some variation in replication times as calculated from the control TSB cultures (mean 28 min. s.d. 4 min). The variation in replication times was not related to the length of storage.

Two major factors contribute to this variation: 1) the cultures must be removed from the incubator once every hour for scintillation countings and 2) we are forced to use a two-hour interval for calculation of replication times. More frequent counting would allow more precise determination of K, but would further decrease incubation time. The solution to these two problems is to modify, as Buddemeyer has, the scintillation counting system such that the sample chamber is heat controlled. Such modification would have four distinct advantages: 1) constant incubation of specimens, 2) elimination of need to manually remove specimens from the incubator and thus further reducing technician involvement, 3) more frequent counts, and 4) continuous computerized monitoring of the growth kinetics.

The ability to graphically depict the logarithmic growth phase and calculate replication times provides us with the opportunity to more accurately assess the kinetics of bacterial growth. The ability to accurately assess the growth kinetics, in turn, allows the appreciation of large as well as subtle differences in growth patterns. To demonstrate these differences by plate count or turbidity techniques would be considerably more time consuming and technically more difficult.

It has been shown that amniotic fluid contains sufficient nutrient to support bacterial growth [7]. Our study supports this conclusion. Three out of the five amniotic fluids presented in Fig 3 have accelerated growth phases similar to the control TSB's.

There is a similarity between the growth curves seen in the various amniotic fluids (Fig 4 A-E) and those curves seen in Fig 4F with the various known concentrations of a bacterial growth inhibitor. This supports the work of others who have demonstrated bacterial growth inhibitors in amniotic fluid.

The purpose of this presentation is to show how a previously reported radiometric method for measuring bacterial growth can be adapted to the study of bacterial growth in amniotic fluid. Our experience with the method, we feel, justifies its continued use as a laboratory tool in the experimental investigation of bacterial growth. Its two main advantages are that it provides rapid, sensitive, dynamic data and involves less technician time than that needed in plate count methods. Modification and computerization of the scintillation counting system could further reduce the demand on laboratory personnel. The study of bacterial growth patterns in amniotic fluid is but one adaptation of this radiometric method currently under investigation in our laboratory. We are accumulating data in an attempt to correlate lack of bacterial growth inhibition in amniotic fluid with subsequent amnionitis.

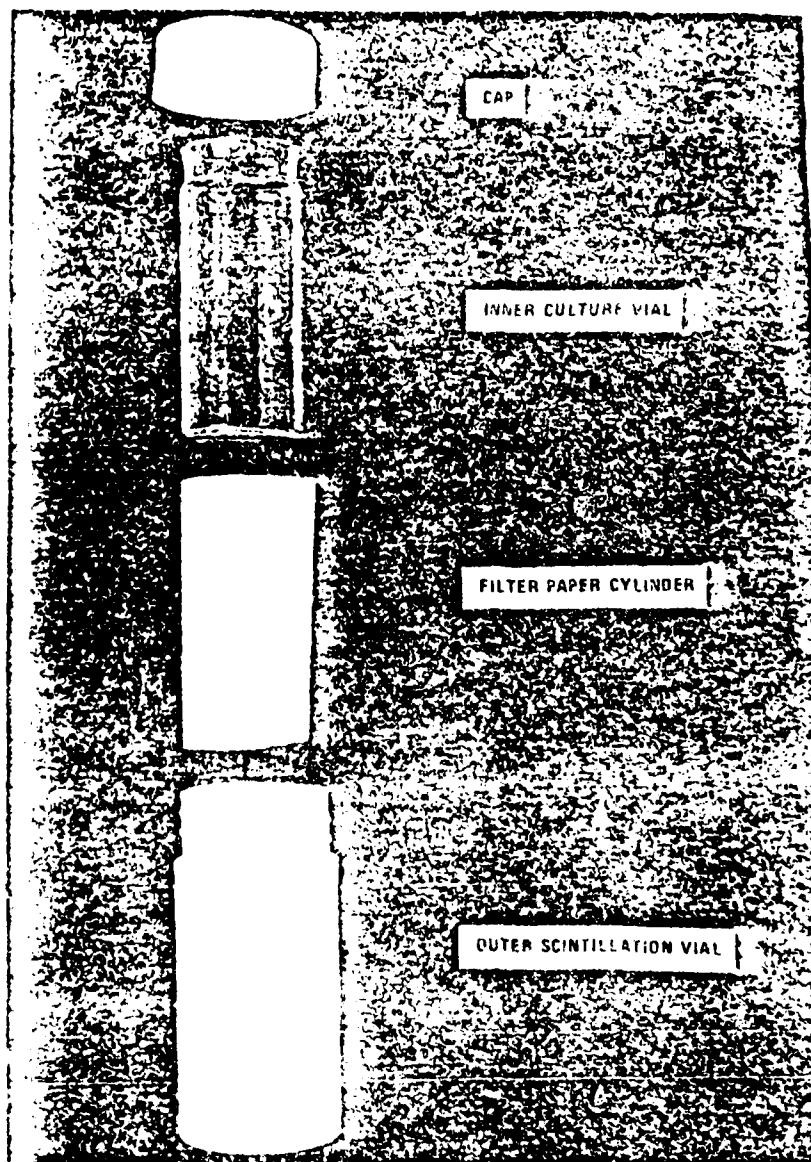


Fig. 1 Metabolism and Culture Chamber. Filter paper cylinder and inner culture vial fit inside the outer scintillation vial. The cap fits the outer scintillation vial.

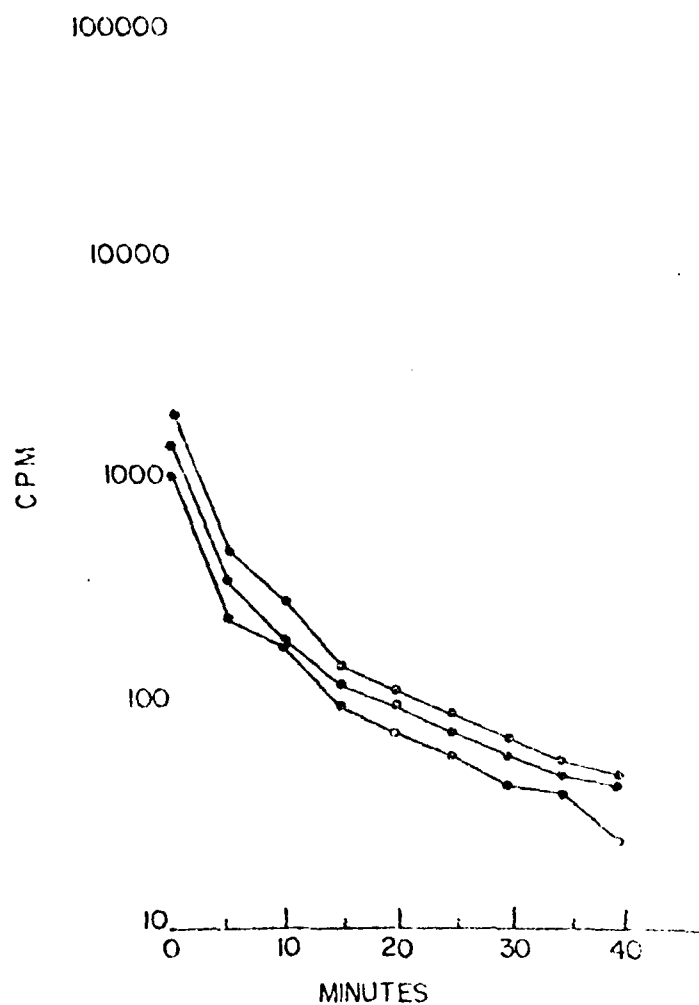


Fig. 2 Incident light effect on the filter paper "fluor". Scintillation counts were down to background level within 40 minutes.

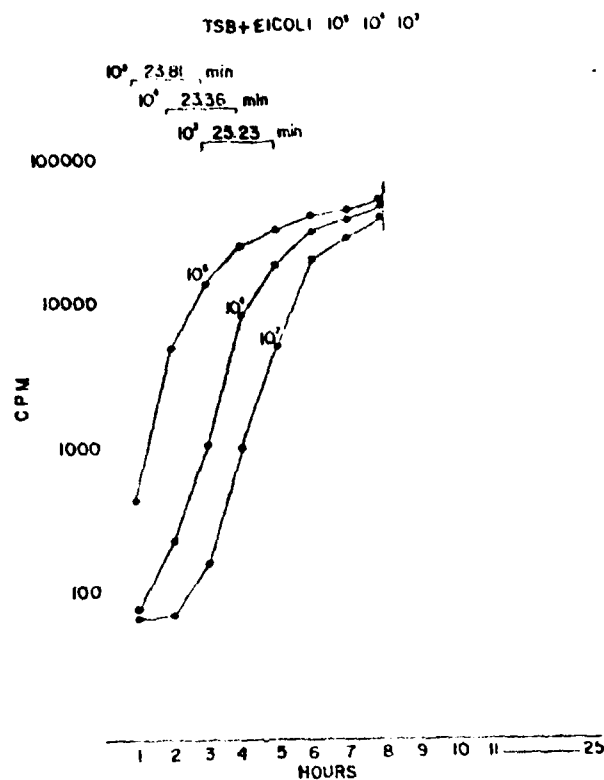


Fig. 3. Growth curves of *E. coli* (0.1 ml inoculum) 10^6 , 10^4 , 10^2 organisms/ml in TSB. Figures at the top of the graph indicate the replication times and the corresponding 2 hour time interval over which they were calculated

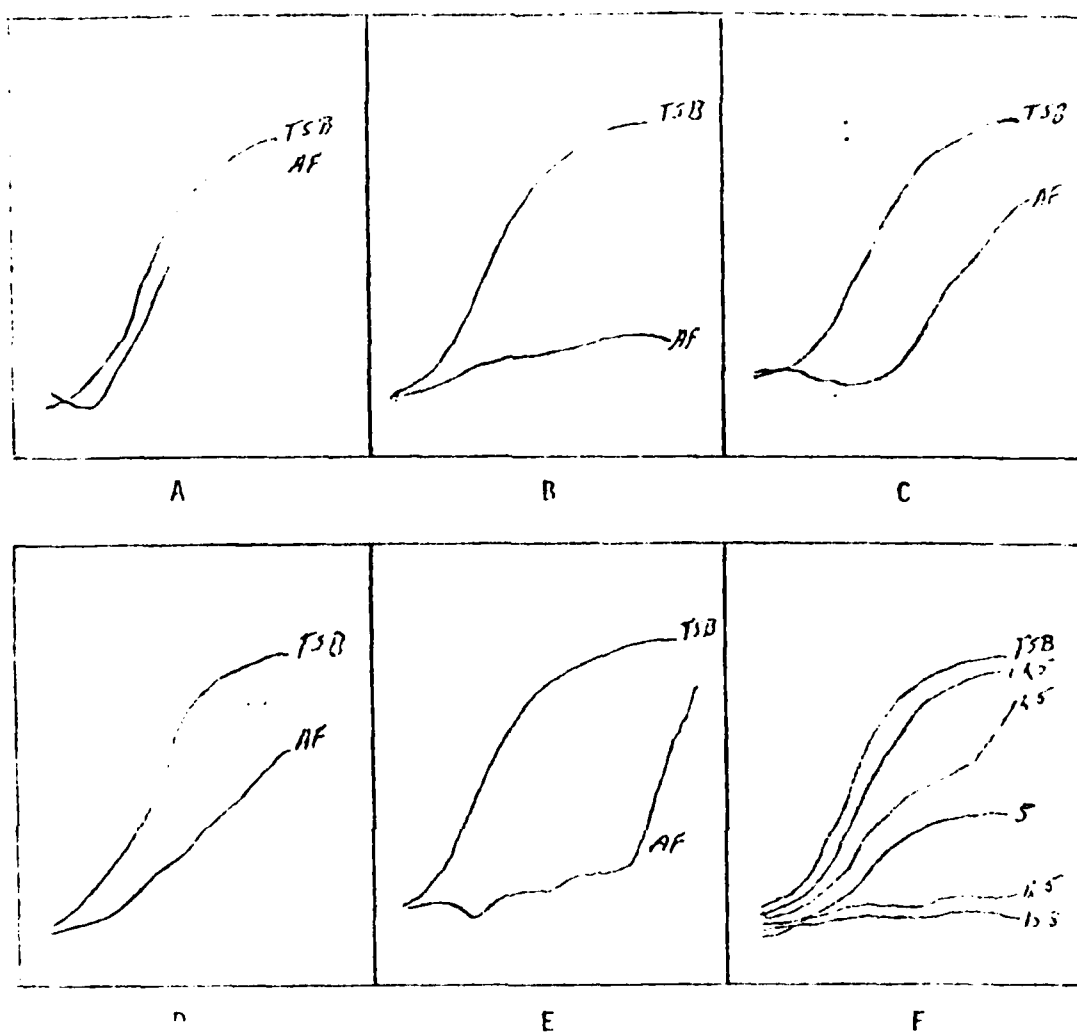


Fig. 4. Graphed data depicting representative growth patterns in various fluids. A. no inhibition. B. complete inhibition. C. short lag phase. D. generally slow growth. E. prolonged lag phase. F. growth curves of *E. coli* in TSB to which various concentrations of ampicillin have been added (curve labeled TSB has no ampicillin). Number at the top of the graph A through E are the calculated replication times and (——) represents the 2 hour interval over which the times were calculated. Replication times for F appear in Table I.

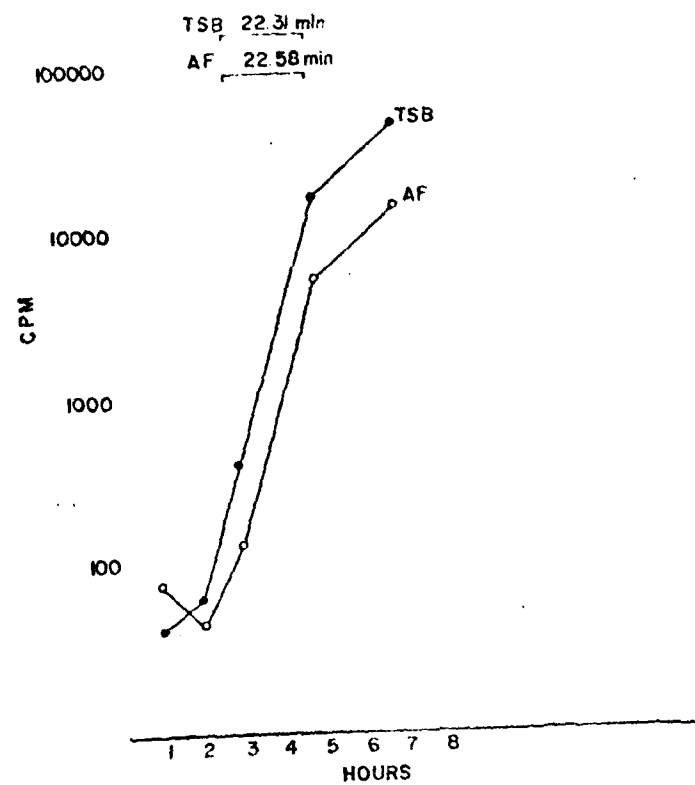


Fig. 4 A

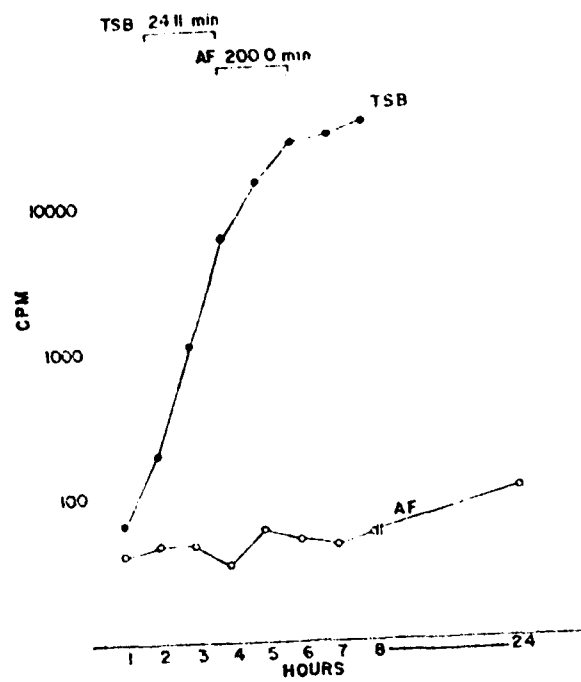


Fig 4 B

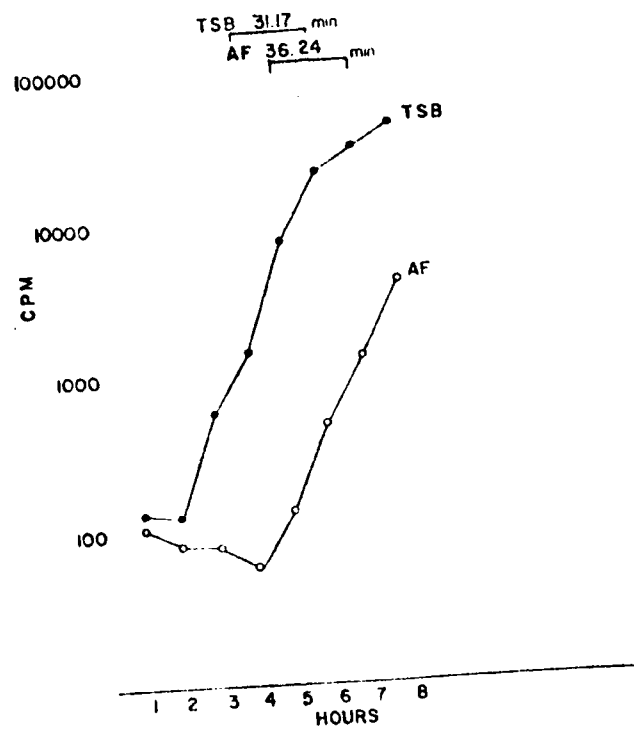


Fig. 4 C

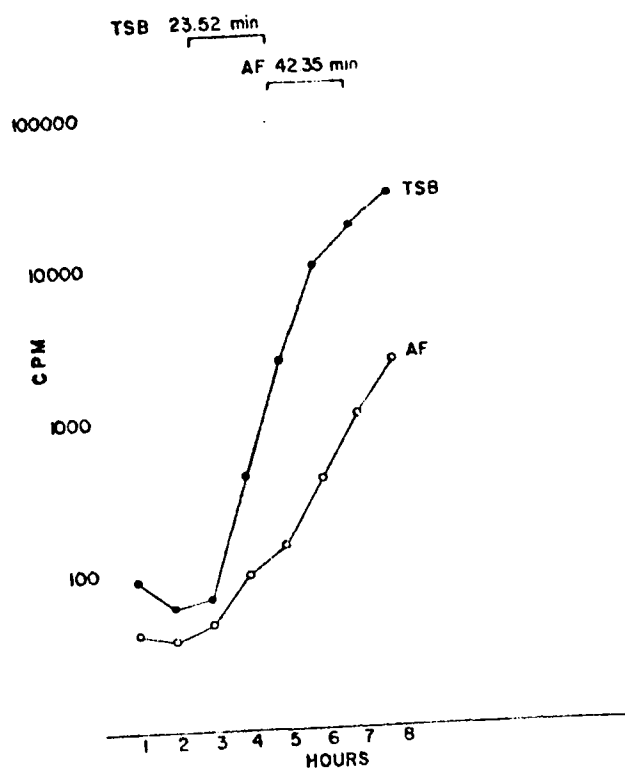


Fig 4 D

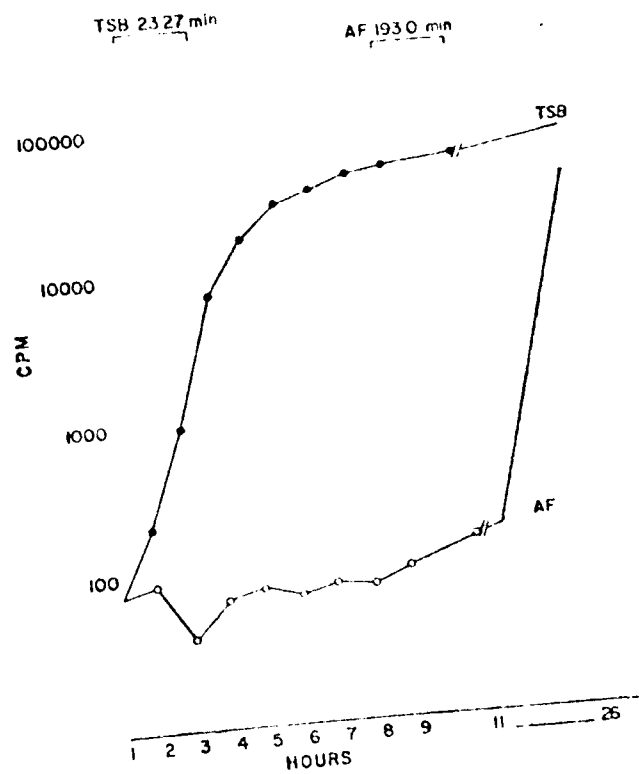


Fig. 2

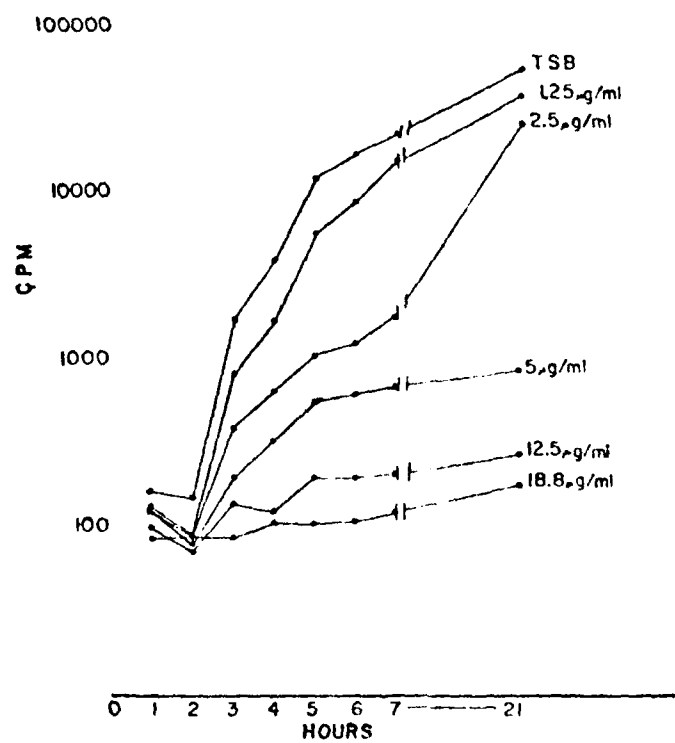


Fig 4 F

Table 1. Various concentrations of ampicillin in TSB and the corresponding *E. coli* replication times

ampicillin conc. $\mu\text{g/ml}$	0	1.25	2.5	5.0	12.5	18.8
replication times in mins.	25.0	28.3	41.8	58.5	187.3	375.0

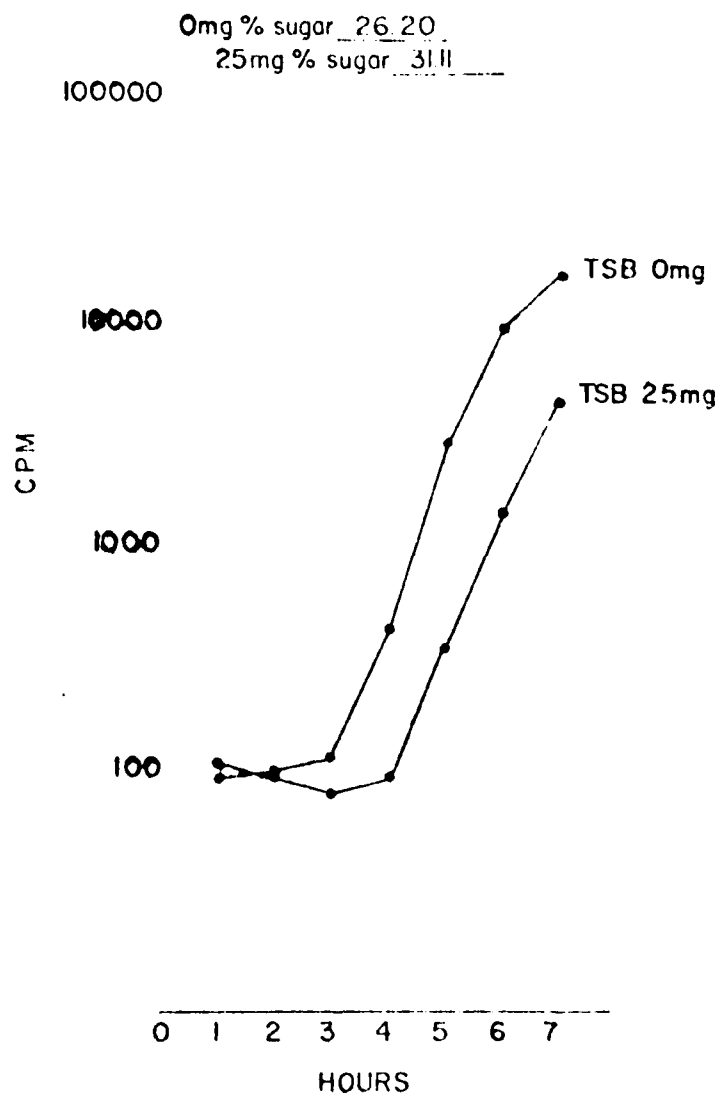


Fig. 5 Growth curves of *E. coli* in TSB with and without non-tagged glucose

STATUS: ONGOING

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Effect of Prostaglandin Synthesis Inhibitors on Uterine Blood Flow

WORK UNIT NO: 77/19

PRINCIPAL INVESTIGATOR LTC W. C. Daniell, MC

ASSOCIATE INVESTIGATORS: B.E.F. Reimann

OBJECTIVES

Determine effects of prostaglandin synthetase inhibitors on uterine blood flow in pregnant animals.

TECHNICAL APPROACH

Attempt was made to measure effects of cannabinoids, indomethacin and aspirin on uterine blood flow in dogs.

PROGRESS

Dogs are poor experimental models for studying uterine blood flow. Five beagles were studied with inconclusive results.

STATUS: Awaiting revision of facility in order to be able to do work on pregnant ewes.

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Efficacy Study of (15S)-15 Methyl Prostaglandin F2a(tham)
(U-32,921F) for Abortifacient Activity by IM, Administration
in Cases of Failed Abortion by Other Means

WORK UNIT NO: 77/23

PRINCIPAL INVESTIGATOR COL W.N. Otterson, M.D.

ASSOCIATE INVESTIGATORS: COL D. Boyce, M.D., CPT R. George, M.D.

OBJECTIVES

To determine the efficacy of (15S)-15-methyl Prostaglandin F2a(tham) as an abortifacient by IM administration for failed second trimester abortion following intra-amniotic injection of Prostaglandin.

TECHNICAL APPROACH

Patients desiring second trimester abortion will be counselled and selected for this study following their signing of a voluntary agreement to participate in this study. Forty milligrams of Prostaglandin F2a will be injected intra-amniotically. If this method fails to accomplish the second trimester abortion within 24 hours, the intramuscular 15 methyl Prostaglandin F2a will be administered according to protocol. Hemagram, urinalysis, clotting studies and vital signs will be monitored prior to, during, and at the termination of the abortion.

PROGRESS

Twenty-four patients were studied. Data was presented at the Armed Forces District Meeting, American College Obstetrics and Gynecology, October 1978. A manuscript is being submitted for publication and is excerpted below:

From 1 November 1977 through 15 July 1978, 24 patients were treated with 15-methyl PG F_{2a}. Four of these patients did not fully meet the criteria of the protocol and are not included in the statistical calculations but will be discussed later. The remaining 20 patients were between 16 to 20 weeks' gestation (determined by last menstrual period and/or uterine size), were admitted for a second trimester VIP and failed to abort with 24 hours following the intra-amniotic injection of 40 mg PG F_{2a}.

Complete abortion was said to occur when (a) embryonic and placental contents of gestation had been expelled in their entirety or (b) when an incomplete abortion proceeded to completion without the need for full surgical intervention. The removal of the products of conception manually or by sponge forceps from the vagina or dilated cervical os without the need for full surgical intervention was regarded as a complete abortion.

Incomplete abortion was said to have occurred when the retained products of conception had not been expelled in their entirety and surgical evacuation of the uterus was required to complete the abortion.

Contraction onset was that time from the first intramuscular injection of the 15-methyl PG F_{2a} to when the patient became aware of uterine cramping.

Treatment-expulsion interval was that time from the first intramuscular injection of 15-methyl PG F_{2a} to complete or incomplete abortion.

All patients were pretreated one hour prior to the initiation of 15-methyl PG F_{2a} with oral Phenergan (R) 50 mg and Lomotil (R) 2 tablets. Vital signs (BP, TPR) were taken prior to initiation of therapy and every hour thereafter until abortion was complete. Blood was drawn for hematocrit, hemoglobin, white cell count, differential and platelet count prior to the first injection, 8 and 24 hours after initiation of 15-methyl PG F_{2a} therapy.

Patients received 250 ug 15-methyl PG F_{2a} intramuscularly every 3 hours until abortion was complete or for a maximum of 5 injections. If abortion had not occurred, dosage was increased to 500 ug every 3 hours until abortion was complete, or for a maximum of 5 injections.

The overall range of time from the first injection to abortion was 30 minutes to 17 hours, 45 minutes with a mean time of 5.06 hours \pm 5.4 hours sd. Although there appeared to be a progressive decrease in the average injection to abortion times related to weeks of gestation, regression analysis showed no significant relation ($R = 0.27$).

The abortion interval was significantly shorter if the membranes were ruptured at the onset of 15-methyl PG F2a therapy. The usual side effects of nausea, vomiting and diarrhea associated with prostaglandin therapy did not appear to be a problem. Five of the 20 patients in this series had vomiting or diarrhea and this was limited to one episode per patient. No patients with a history of asthma were encountered in this series and there was no observed respiratory distress during therapy in any of the treated patients.

Blood loss appeared to be minimal. Estimated blood loss ranged from 50 cc to 400 cc with an average of 150 cc.

Hyperpyrexia was not observed in these 20 patients. One patient who had ruptured membranes following the intra-amniotic instillation of PG F2a developed evidence of amnionitis and had a temperature of 102°F. prior to initiation of the 15-methyl PG F2a. Otherwise the highest temperature was 100.4°F.

All patients had a suction curettage following expulsion of the products of conception regardless of whether the abortion was felt to be complete. Seven of the 20 patients, however, were felt to be incomplete and required suction curettage to complete the abortion.

It is difficult to determine from antecedent literature what the success rate is at 24 hours and more pertinent, the complication rate of the first 24 hours compared to the second 24 hours. It would appear that about 50-60 percent of abortions are complete 24 hours after intra-amniotic instillation of PG F2a. During the period of this study 43 patients 16-20 weeks gestation admitted for voluntary interruption of pregnancy were treated with 40 mg PG F2a intra-amniotic. Twenty-three were complete by 24 hours (53.5%).

Complications in the form of infection and blood loss appear to be related to the length of the abortive process, the presence of ruptured membranes and the need for repeated intra-amniotic injections. Therefore, to consider an abortion method failed after 24 hours and the institution of an effective secondary method would seem reasonable.

Rupture of the membranes associated with intra-amniotic instillation is a frequently occurring problem. This complication prevents repeat amniotic instillations and increases the risk of amnionitis. Five of the 20 patients (25%) had ruptured membranes prior to the initiation of the 15-methyl PG F2a and had a significantly reduced abortion interval. None of the patients received an oxytocin infusion during the abortive process.

The age range was 15 to 29 years. There were 13 nulliparous and 7 parous patients. As has been the experience of others, we could find no significant difference in abortion times related to age or parity. The four patients who received intramuscular 15-methyl PG F2a and not included in the study series are summarized in Table 2. The first two patients (C.A. and L.O.) did not fit the protocol in that multiple attempts at amniocentesis failed and therefore they did not receive an intra-amniotic injection of PG F2a. The first patient (C.A.) was extremely anxious and the nausea and vomiting (no diarrhea) was felt by the ward personnel to be related to the patient's emotional status and not to the drug itself. The third patient (A.D.) was only 14 weeks and although she was given 40 cc of PF F2a, there was considerable question as to whether it was intra-amniotic. The fourth patient (K.A.) was admitted with evidence of an abruption and an intrauterine fetal demise. When she failed to abort with 2 prostaglandin E2 vaginal suppositories, it was decided to use the 15-methyl PG F2a intramuscularly. She had a significant drop in fibrinogen and platelets with an estimated 2500 cc blood loss. The DIC was felt to be related to the placental abruption and not to the PG therapy.

The average abortion interval and total dosage in these 4 patients was far greater than that required by the other 20 patients. Although it can be argued that these 4 patients did not have the benefit of intra-amniotic PG F2a, 24 hours prior, it is our impression, based on limited experience, that intramuscular 15-methyl PG F2a is not best utilized as a primary abortifacient.

Nausea, vomiting and diarrhea occurred in 25% of the patients and were easily controlled. It is our impression that these side effects were greater with the intra-amniotic instillation of PG F2a. It is also worth mentioning that the intramuscular injection of the 15-methyl PG F2a was not associated with complaints of pain at the injection site.

It would appear that 15-methyl prostaglandin F2a is (1) an effective secondary abortifacient, (2) is most effective in the presence of ruptured membranes, (3) is relatively free of side effects in the dosage range used in this study.

TABLE 1

Effect of Membrane Status		Range	Mean + sd	N
Intact	0.5 - 17.75 hrs		7.4 + 5.52	15
Ruptured	0.5 - 3.15 hrs		1.65 + 1.009	5
			$p = < 0.01$	

Patient	Age	Para	Weeks Gest.	Total Dosage	Abortion Interval	Remarks
1. C.A.	21	0	16	1000 ug	10.0 hrs	Severe nausea/vomiting
2. L.P.	18	0	16	4500 ug	40.75 hrs	No complication
3. A.P.	27	3	14	3700 ug	32.25 hrs	Temperature to 101 ⁸
4. K.A.	21	0	20	1750 ug	16.5 hrs	Abortion with DIC
		Average		2750 ug	24.88 hrs	

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: A Comparison of Phospholipid Levels and Choline Phospho-
transferase (CPT) Activity in Amniotic Fluid and Newborn
Trachael Fluid

WORK UNIT NO: 77/25

PRINCIPAL INVESTIGATOR LTC L.L. Penney, M.D.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if the level of phosphatidyl glycerol (PG) and phosphatidyl inositol (PI) or the activity of choline phosphotransferase could serve as an accurate index of lung maturity.

TECHNICAL APPROACH

Amniotic fluid, and neonatal gastric and pharyngeal fluids which are normally discarded, will be analyzed for phosphatidyl glycerol, phosphatidyl inositol, choline phosphotransferase, and magnesium. The levels measured will be correlated with the incidence and severity of neonatal respiratory stress and hyaline membrane disease.

CONSUMABLE SUPPLIES

\$1270

PROGRESS

Biochemical techniques for rapid separation of PG have proven to be difficult to reproduce. Further evaluation is in progress, but reproducible results have been obtained. Clinical specimens are now being solicited.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Fetal Movement as an Indicator of Fetal Well Being

WORK UNIT NO: 77/26

PRINCIPAL INVESTIGATOR MAJ Walter Daniell MD

ASSOCIATE INVESTIGATORS: COL A. Killam MD, MAJ T. Howard, MD

OBJECTIVES

To determine if quantitation of fetal movement is a reliable indicator of fetal well-being comparable to estriols and the oxytocin challenge test.

TECHNICAL APPROACH

Patients admitted to the Antepartum OB Ward who are being monitored by urine or serum estriol and oxytocin challenge tests will be asked to participate in this study. They will be instructed to count and record the number of fetal movements that they feel each hour between 0800 hours and 2200 hours. Changes noted in fetal movement will then be compared with changes in the estriols, the OCT, and the ultimate fetal outcome to determine if changes in the number of fetal movements is a predictor of intrauterine fetal distress that could be comparable to or better than present methods being used. Fetal movements counted each day will be compared to those counted each hour to determine if shorter time periods for counting fetal movements would be of value.

PROGRESS

The project was terminated by the principal investigator as, by the time approval was received from OITSG, the subject had been well studied elsewhere. Fetal movement tests have been shown to correlate well with other tests of fetal well being.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

Comparison of Usual Clinical and Laboratory Measurements of
TITLE: Gestational Age with Gestational Age Determined by Radioreceptor
Assay (RRA) for HCG

WORK UNIT NO: 78/07

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To confirm the accuracy of pregnancy dating within the first to fourth weeks following ovulation reported by others with the use of RPA for HCG. To correlate this data with other parameters of fetal age as an assessment of the accuracy of these tests which heretofore have relied on subjective, variable gestational age estimates (i.e. menstrual cycle length, LMP, etc.)

TECHNICAL APPROACH

The study will be run as an adjunct to protocol 76/20, with additional volunteers selected from the routine obstetrical clinic. The HCG values will be determined by commercially available RRA. These values will be available only to the principal investigator until the conclusion of the study, at which time the test, if justified, may be instituted as a routine study.

CONSUMABLE SUPPLIES

\$1605

PROGRESS

In establishing baseline data for this protocol serum estriol, an accepted laboratory parameter of gestational age, has been re-evaluated. The work regarding the unconjugated fraction has been submitted for publication and is summarized in the following paragraphs:

Thirty-four patients were studied in a longitudinal manner following informed consent. All of the pregnancies were normal and gestational dates were accurate. Only patients whose menstrual cycles were 28-30 days in length and who had pelvic examinations to confirm uterine size in the first trimester were selected. Gestational age from quickening, first audible fetal heart tones, and newborn examinations were all consistent with the established estimated dates of confinement.

Thirteen of the patients were studied weekly from 32 or 33 weeks gestation to 38 or 39 weeks. The remaining 21 patients were studied daily beginning at week 35 and continuing for 12 to 15 days. Antecubital venous blood specimens were drawn between 0900 and 1500 hours for the group. Since diurnal variation is still controversial, individual patients were sampled within one hour of the same clock time at each visit. After formation of the clot at 4°C and centrifugation serum was removed and stored at -20°C until use.

Dated specimens from all patients were logged sequentially and assigned random numbers generated from a standard table. The technician performed each run sequentially using the random, rather than the chronological, numbers. All samples from an individual were included in a single assay with the exception that unknowns with a percent difference > 15 in the duplicate tubes were empirically rejected and repeated. The repeat rate was 1.6%. The median coefficient of variation between replicates for 372 unknowns was 6.4%.

Antiserum, estriol standards and 125I labeled estriol were supplied by Amersham Corp., Arlington Heights, Ill. The % cross-reaction at a steroid concentration of 100 ng/ml has been extensively tested by the manufacturer. Selected values are: estrone 0.1, estradiol 1.3, estetrol 27.6, 16-epiestriol 7.7, 17-epiestriol 0.3, 16,17-epiestriol 0.2, estriol-3-sulfate 2.4, estriol-3-glucuronide 2.3, and estriol-16-glucuronide 0.1. The manufacturer's comparison of the free estriol assay values before and after diethyl ether extraction produced a line with slope 1.02, intercept = 0.95 and $r = .92$ for 100 samples.

The assay was modified only to include a total count tube and a nonspecific binding (NSB) tube with each run. The NSB tube substituted male serum for sample but was otherwise identical to the patient tubes. The standard tubes in this assay also use human serum. Counting was performed on a Searle Model 1285 Automatic Gamma Counter.

Five methods of data reduction were investigated. Linear spline and log spline fits were least accurate and precise judging from control samples. Manual calculation consistently underestimated known high values. A weighted logit-log program was purchased through the Hewlett-Packard Corp. for use on a Model 9845 desktop

computer. The weighting coefficients of $a_0 = .001$ and $a_1 = .003$ were not changed during the study. The standard deviations (SD) were identical if computed by weighted logit log or unweighted logit-log. The latter method was arbitrarily selected as it had the greatest range due to higher estimates of the upper end of the dose curve.

Two runs during the course of this study had %NSB values > 3 SD above the previous mean and these assays were repeated in toto. The stability of the 18 accepted assays was monitored by the 9 parameters shown in Table 1. Fifteen assays were within $+ 2$ SD of the mean on all 9 parameters. Assay 2 had a minimum detectable dose of .456 ng/ml ($+2.8$ SD). Assay 10 had a slope of -1.406 (-2.5 SD) and % NSB of 5.2 (-2.9 SD). Assay 15 had a % Bo/T of 61.2 ($+2.2$ SD). Two quality control sera were included in each run yielding means of 7.1 ± 0.5 and 18.2 ± 1.9 . For the low control within assay coefficient of variation was 4.9% and between assay coefficient of variation was 7.0%. The corresponding figures for the high control were 2.7% and 10.4% respectively.

In addition the low and high control were each analyzed ten times in succession following the unknowns during one of the runs as an indicator of within assay systematic drift. The usual control replicates preceded the unknowns.

Analysis of variance comparing nontransformed, exponential, quadratic, and power regression models for linearity revealed the first two to be preferable with a slightly more statistically significant F-ratio for the exponential transformation than for the raw data in both groups. All further data reduction uses the logarithmic value of the serum free estriol concentration.

The regression lines of the two data sets individually and collectively do not differ significantly in slope or intercept. The lowest points at 34 weeks, 35 weeks, and 35 weeks 2 days were eliminated and again individual and collective regression lines were computed. None of the excluded points fell below the 95% confidence interval for the altered regression lines. The 36 week, 37 week, and 36 week 2 day data points fell within the 95% confidence interval predicted from the regression lines through 35 weeks.

The apparent nadir in the data at 35 weeks 2 days was only marginally different than the apparent peak at 36 weeks 2 days by the student t-test ($t = -01.97$, 39df, $.025 < P < .05$). Moreover, by computing regression lines of three or more points, but using all possible combinations of available data from 32 or 33 weeks through 35 weeks 2 days, no lines were found with upper limits that excluded the subsequent 36 week 2 day point or any later points.

A significant difference in slope was hypothesized and the five lines with the least positive slope through 35 weeks 2 days were compared with five lines from 35 weeks 2 days through 37 weeks selected for the most positive slope and containing at least three points. The 25 slope comparisons revealed no differences ($P > .1$ in all cases). A hypothetical slope of zero through 35 weeks comprised of 300 data points with S_{yy2} of 0.01 and S_{x2} of 0.01 does not differ from the calculated slope of the 278 daily data points from 35 to 37 weeks in this study.

Individual patients were studied by computing the regression line from the first three data points and iterating searching for an ensuing value which exceeded the 95% confidence interval predicted for the next point in the sequence. Two of thirteen patients sampled weekly exhibited this phenomenon. The event occurred at 35 weeks in both cases. The finding of a surge calculated in this manner in only 2/13 patients between 35 and 37 weeks is clearly discordant with the 100% (9/9) and 96% (48/50) reported by Buster and by Sakakini.

The concept of an inflection point in the progressive increase in maternal serum free estriol during the third trimester of pregnancy has obvious implications as a low risk, simple method of determining gestational age. If such a change occurs and is to be clinically useful, it should reasonably meet certain criteria among which are those tested in this report. 1) Most apparently, since its main usefulness would be in those patients seen late in their antepartum course, it should occur reproducibly within a few days in every normal pregnancy so long as three or more samples are available to estimate the regression line. Ideally pooling of several samples drawn over a short time period for single data points would not be necessary. 2) Correlation coefficients, or more properly r^2 , should indicate the variation in estriol is primarily a function of linear regression on weeks. Thus the inflection should also be present in the means from samples collected in a longitudinal manner whether or not the assay sequence is randomized. 3) The inflection should be apparent with any satisfactory assay methodology or curve-fitting procedures. Furthermore, if this is a real phenomenon one could 4) expect an increase in slope from the nadir to the surge point, compared to the slope from origin to nadir, or, if the slope remains unchanged, an increase in the intercept comparing post-surge to pre-surge regression lines. Since the latter possibility would require at least seven points at weekly intervals, and could not be calculated until near term, it was deemed impractical, even if real, and not investigated further.

Although the data is valid by several quality control parameters, the r value, .598, for the combined weekly data is considerably lower than the .997 reported by Buster et al. The variation in our patients week to week however is similar to that reported by other authors and by Buster in a subsequent publication. Furthermore the larger mean r of .726 computed from averaging the 13 r values from the individual regression lines indicates less within patient than between patients variation unaccounted for by regression on weeks. One could expect a dependence of the surge as much on narrower confidence intervals for a predicted Y (estriol) as a function of increasing N (number), as on deviations from regression on X (length of gestation). Results from individual patients sampled daily were consistent with this supposition. Five of 21 exhibited a "surge" - in all cases at the seventh data point or beyond. Simultaneously reducing N (widening confidence interval for next predicted Y) and smoothing day-to-day variability by pooling of successive data points in groups of two (narrowing confidence interval for next predicted Y), eliminated these "surges". It would seem possible that pooling of several specimens drawn a few minutes apart combined with sampling more often than weekly for several weeks might accurately define a surge if one exists. This would, of course, reduce clinical practicality.

The assay used in this report is of a type readily available to many laboratories. It is stable enough by several parameters to indicate data variation does not reside primarily in the method. The unweighted logit-log was selected to deliberately introduce bias toward demonstrating a surge as this method computed higher values at the upper end of the curve as well as computing the greater range.

Manipulation of the data to seek the extremes still failed to demonstrate any differences in slope between lines terminating, and lines originating, at the nadir. In fact only a negative slope from 32 to 35 weeks would differ from the calculated slope between 35 and 37 weeks. Such a decline in estriol concentration has not been reported to the author's knowledge. Even the 36 week 2 day point, which nears the upper predicted 95% confidence interval for the five arbitrarily selected lowest slope lines and is different than the 35 week 2 day point by t -test, cannot be rejected as an outlier.

During the chronological period studied the increasing maternal serum free estriol as a function of time may be adequately described as exponential. Although greater correlation exists with length of gestation in individual patients singly sampled for each data point than in the means, the variability both within patients and between patients is substantial. The magnitude of this variability obscures any reproducible relationship between a given fluctuation in the serum free estriol and advancement of gestational age for this condensed time frame and correspondingly small N . This failure to confirm an inflection point coinciding with length of pregnancy persists despite deliberate attempts to bias the data in favor of such a phenomenon.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Acid Aspiration Prophylaxis with Cimetidine, Glycopyrrolate,
and Antacids

WORK UNIT NO: 78/08

PRINCIPAL INVESTIGATOR LTC W. Daniell, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

This study will determine the relative effectiveness of three different preoperative premedication protocols in reducing the risk of acid aspiration before, during, and after routine surgical procedures.

TECHNICAL APPROACH

The effects of premedication prior to surgery on gastric juice volume and pH will be evaluated in 200 patients undergoing elective nongastric surgical procedures under general anesthesia requiring intubation. Patients taking medications that alter gastric secretion or who have had a history of gastric surgery will be excluded. All patients will be NPO from 2300 the day before surgery. The patients will be randomly assigned to four treatment groups. The data to be analyzed will consist of age, weight, sex, type of premedication, type of surgery, type of anesthesia, length of surgery, observed aspiration, and pH and calculated gastric secretion volume of intubation and extubation collections.

PROGRESS

The staffing shortage in Anesthesia has precluded institution of the study. Patients will be entered if conditions permit.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEALMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: RhoGam Monitoring; Fetaldex versus Detection of Circulating
Anti-Rho(D)

WORK UNIT NO: 78/10

PRINCIPAL INVESTIGATOR MAJ M. Sellers, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare testing for anti-D antibody in the serum of Rh negative women receiving human anti-D gamma globulin for the prevention of Rh sensitization with the Fetaldex test for fetal RBC in maternal blood.

TECHNICAL APPROACH

Fetaldex tests and the standard test to determine if anti-D antibodies are present in the patient's blood 24 to 48 hours after the RhoGam will be done and the results compared. When possible Rh sensitization will be tested for at 6 to 9 months after delivery.

PROGRESS

Sample acquisition continues to proceed slowly.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Role of Prostaglandins and Prostaglandin Synthetase
Inhibitors in Hemorrhagic Shock

WORK UNIT NO: 78/11

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if prostaglandin levels are increased during hemorrhagic shock and if prostaglandin synthetase inhibitors improve or worsen an animal's condition in hemorrhagic shock.

TECHNICAL APPROACH

Hemorrhagic shock is induced in the standard method of Hardaway. Serial determinations of prostaglandins and the standard physiologic parameters. Some of the animals will be given a saline placebo, others will be given a prostaglandin synthetase inhibitor.

CONSUMABLE SUPPLIES

\$37

PROGRESS

The principal investigator Col Killam has retired and has been replaced by the associate investigator. Techniques for quantification of the major prostaglandins from plasma are now available in the Clinical Investigations Service, but no animals have been studied to date.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Inhibition of the Vascular Effect of 17β -Estradiol with
Actinomycin D

WORK UNIT NO: 78/26

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if the vascular effect of 17β estradiol employs the same pathways as the growth promoting effect on the sex organs of rabbits.

TECHNICAL APPROACH

Actinomycin D will be given to rabbits in sufficient dosage to block the growth promoting effect of estradiol 17β , which is a potent vasodilator of the uterus as well as a potent growth promoter. If the vascular effect of estradiol- 17β is not affected nearly as much as the growth promoting effect, this would suggest that the vascular effect does not rely on transcription. Thirty rabbits will be divided into five random groups, all will initially have their ovaries removed. A minimum of thirty days will be allowed to elapse before studying the animals. A femoral vein and artery and a carotid artery will be catheterized. Baseline uterine blood flow will be determined by infusing 10-15 μ Ci 141 Ce microspheres in the carotid catheter and sampling from the femoral artery. One μ g/Kg of 17β estradiol with labeled uridine and amino acids will be given IV and the control animals subdivided for study at hourly (or less if needed) intervals to determine onset of increased blood flow. An infusion of 30-40 μ Ci 51 Cr at these intervals will be used to calculate blood flow. All animals will then be sacrificed and aliquots of uterine tissue for RNA and protein quantitation and label incorporation will be analyzed. The microspheres per gram of uterine tissue and per organ will be determined. Subsequent repeat blood flow studies will be done at the earliest time at which control animals increased their uterine blood flow. These animals will receive actinomycin 8 mg/Kg, cycloheximide 4 mg/Kg, a combination of these two, or puromycin 200 mg/Kg 30 minutes prior to hormone administration.

PROGRESS

The project remains suspended pending further funding.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Distribution of Group B Streptococcus

WORK UNIT NO: 78/27

PRINCIPAL INVESTIGATOR MAJ R. Heath, M.D.

ASSOCIATE INVESTIGATORS: Robert Frederick, PhD

OBJECTIVES

To determine where Group B Streptococci are sequestered in the body of rabbits after intravenous infusion.

TECHNICAL APPROACH

Approximately 24 rabbits will be given Group B strep grown in media containing P³² phosphate to make the organisms radioactive. The rabbits will be sacrificed at 15 minutes, 1 hour, or at 12 hours after the injection. Half will be given live organisms and half will receive killed organisms. The blood, lung, heart, liver, spleen, brain, bowel (jejunum), adrenal lymph nodes in the mesentery and para-aortic area and thigh muscle will be removed and a portion prepared for microscopic evaluation and autoradiography. The remainder of the organs will be counted in the liquid scintillation counter for radioactivity. The amount of radioactivity in the 15 minute group will be compared with the one hour and 12 hour groups to see where the majority of the organisms are sequestered immediately after infusion and to see if the radioactivity of the organisms is redistributed from its initial position in the body.

CONSUMABLE SUPPLIES

No new purchases in FY79
\$1000 in FY78

PROGRESS

Sufficient study has been accomplished to show reticuloendothelial uptake with no significant alterations occurring later. We are now moving to establish bacterial clearance rates utilizing this same approach.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Prevention of Post Cesarean Section Infections

WORK UNIT NO: 79/04

PRINCIPAL INVESTIGATOR: LTC W.C. Daniell, MC

ASSOCIATE INVESTIGATORS: Dr. Knudson

OBJECTIVES

To determine whether the routine administration of Cephalin will lower the incidence of post-cesarean section infectious morbidity. There is a 30-40% incidence of infectious morbidity if a woman is delivered by cesarean section following labor with ruptured amniotic membranes for longer than six hours. Prophylactic administration of antibiotics to patients undergoing vaginal hysterectomy has significantly reduced the rate of infectious morbidity. It is hoped that an antibiotic regimen can be discovered which will reduce the infectious morbidity associated with cesarean section. The cephalosporins have been used extensively for prophylaxis with vaginal hysterectomy. Cephalin was chosen because a single dose given prior to vaginal hysterectomy has been shown to be at least as efficacious as the standard 3 dose regimen with cephaloridine. Other studies involving antibiotics for post-cesarean section infections have not shown a consistent, significant lowering of morbidity. However, patients not in labor or in labor for long periods of time have been included in these studies. We have selected a very high risk population and will test a 1-dose regimen against a control population. Only those patients who have had ruptured BOW, labor, and intrauterine monitoring prior to delivery will be entered in the study group.

TECHNICAL APPROACH

When a woman is entered into the study, she will be placed into one of two drug regimen groups. A control who gets a single injection of a placebo intravenously at the time of cesarean section, another group who gets a single shot of Cephalin, 1 gram IV at the time of cesarean section. Upon discharge, both the mother's and the infant's charts will be reviewed by a member of the perinatal staff and a listing of all the complications compiled from a data sheet included in the study and the chart itself. Patients with previous allergic reaction to penicillin will not be included in the study.

Group I: Placebo at the time of cesarean section.

Group II: Cephalin, 1 gram IV at the time of cesarean section.

Additionally, in conjunction with Dr. Boyce's study on the influence of amniotic fluid on bacterial growth, small samples of amniotic fluid will be obtained through the monitoring catheter which is routinely emplaced upon admission to the Labor and Delivery suite. The inhibitory effect of these individual specimens with particular attention to zinc levels, will be related to the ultimate result in infectious morbidity. We hope to define groups of low and high risk, one group benefitting from prophylactic antibiotic therapy, and the other not.

PROGRESS

Approximately 50 patients have participated in the study thus far, When 100 patients have been entered the code will be broken.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Molecular Etching

WORK UNIT NO: 70/111

PRINCIPAL INVESTIGATOR B.H.F. Reimann, DAC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To obtain general information on the ultrastructure of biological membranes (in particular the erythrocyte membrane) and other cellular organs in order to discern their structural changes under varying experimental (and disease related) conditions and, for this reason, to develop techniques by which the biological material can be investigated in the least altered state employing methods such as freeze drying and ionic etching in conjunction with electron microscopy.

TECHNICAL APPROACH

The final goal is to subject lyophilized embedded biological material to a bombardment with accelerated ions or atoms and to reveal the obtained structures by electron microscopy. Presently the experiments are primarily concerned with osmotic pressures of erythrocytes employing freezing point depression osmometry and direct measurements with a Pfeffer's cell. A "critical point" drying chamber has been constructed.

PROGRESS

Collaboration with members of the Department of Biology, New Mexico State University, Las Cruces, NM, resulted in investigations on cell membranes, cell wall, and mode of cell division in Mycobacterium avium. One publication on this subject is in preparation.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Chemotherapy of Cancer

WORK UNIT NO: 76/07

PRINCIPAL INVESTIGATOR Dr. J. Swaney, M.D.

ASSOCIATE INVESTIGATORS: Dr. V. McKie, M.D.

OBJECTIVES

The association of WBAMC Pediatric Oncology and Hematology Service with the various members of the Southwest Cancer Chemotherapy Study Group, Pediatric Division (through M.D. Anderson Hospital and Tumor Institute), Acute Leukemia Group B, and with the Children's Hospital Oncology Center, Denver, Colorado, in conducting trials of chemotherapy in cancer will (1) obtain the necessary understanding of the cancer process; (2) determine effective therapeutic approaches; and (3) provide needed information to use in the care of children with malignant diseases. The association provides for probing of common knowledge and for better statistical evaluation of processes and results.

TECHNICAL APPROACH

Each protocol used by the various aforementioned groups goes through a rigorous process of review, revision, and evaluation prior to becoming activated for group usage. The flow of protocol from author through specific disease committee, statistician, committee headquarters, studies management board, Cancer Investigation Branch of the National Cancer Institute is the usual process. Data collected by each member is reviewed and analyzed by the individual data sent.

PROGRESS

The patients on the noted protocols continue as previously. The patients remain in continuous remission. The patient on Denver Children's AL#3 ITI has discontinued chemotherapy and is presently NED.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Use of Elliott's B Solution, Sterile as Methotrexate
Diluent for Intrathecal Use

WORK UNIT NO: 76/28

PRINCIPAL INVESTIGATOR: Dr. J. Swaney, M.D.

ASSOCIATE INVESTIGATORS: Dr. V. McKie, M.D.

OBJECTIVES

The object of this study is to determine if the use of Elliott's B solution as diluent for intrathecal Methotrexate will reduce the evidence of side effects, i.e., headaches, fever, vomiting, etc.

TECHNICAL APPROACH

Patients are eligible for this study who are receiving intrathecal Methotrexate either as prophylaxis or for treatment of central nervous system leukemia. Stock solutions of Methotrexate will be diluted to a concentration of 1 mg/cc with Elliott's B solution. The dose of Methotrexate shall be calculated at 12 mg/M² per dose with a maximum of 15 mg/M² per dose. The timing of the intrathecal injection shall be individually determined. Records shall be kept of patient status following injection as regards headache, fever, nausea, vomiting, etc. Response shall be determined by absence of side effects or their diminution if they had been previously present. Possible CNS contamination from injection of foreign material may result in toxicity which may be evidenced by fever, headache, nausea, and/or vomiting following intrathecal injection of Methotrexate diluted with Elliott's B solution. Approximately ten patients per year will be treated on this protocol.

PROGRESS

The patients on the noted protocols continue as previously. The patients remain in continuous remission.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79910

DETAIL SHEET

TITLE: Comparison of Pneumatic Otoscopy and Impedance Tympanometry in
The Followup of Otitis Media in Children

WORK UNIT NO: 76/37

PRINCIPAL INVESTIGATOR LTC R. M. Lampe, M.D.

ASSOCIATE INVESTIGATORS: L. Artalejo, DAC

OBJECTIVES

In cross sectional studies, impedance tympanometry is a reliable screening method for the detection of middle ear fluid in the pediatric age group and compares favorably with pneumatic otoscopy in accurately detecting middle ear fluid. Impedance tympanometry offers an objective measurement of middle ear fluid and its sequential presence or absence following acute otitis media. Comparison of these two methods in the followup of middle ear effusions should demonstrate the utility of impedance tympanometry in the followup of middle ear effusions.

PROGRESS

This study has been summarized for presentation at the Uniformed Services Pediatric Seminar as follows: Tympanometry represents a significant advance in the study of middle ear disease. This technique is a safe, simple, reliable and objective method of determining middle ear function and is felt to be valuable in office screening and in the screening of certain high risk groups. It can also be used as a tool for clinical investigation since it provides an objective measure of middle ear function.

The purpose of this study was to perform tympanometry on pediatric patients with acute otitis media in order to determine if initial tympanometry findings could be related to outcome.

Pediatric patients who had acute otitis media, defined as a red, immobile or bulging tympanic membrane with an absent light reflex, were considered for the study. Patients with ventilatory tubes or cleft palate, patients receiving antibiotic therapy and patients who had an ear infection in the prior three months were excluded. After informed parental consent, patients were given oral ampicillin (100 mg/kg/day, four times daily for ten days) and either placebo or triprolidine hydrochloride/pseudoephedrine (0.05 mg/1.25 mg/kg/day, four times daily) until the tympanic membranes were normal by pneumatic otoscopy and tympanometry.

Tympanometry using a Teledyne TA-1B acoustic impedance meter was done initially and at weekly intervals during the followup period, by the audiologists or physicians involved in the study.

For the purposes of our study, type A tympanograms were defined as those with the peak pressure between +50 and -100 mm water and a normal to high compliance (0.1 to 1.5 cc). Type B tympanograms had no peak pressure and type C tympanograms had a pressure peak greater than -100 mm water.

Physicians performed pneumatic otoscopy and independently recorded whether the tympanic membrane was mobile, mobile retracted, immobile, or bulging. The followup period lasted six weeks. Patients with normal pneumatic otoscopy and a type A tympanogram were considered as therapeutic successes. Patients who had a type B tympanogram after six weeks were considered as therapeutic failures. The antihistamine/decongestant or placebo was continued for six weeks or until tympanometry and otoscopy were normal.

Thirty-two pediatric patients with 43 ear infections were studied between December 1978 and April 1979. Initial tympanometry demonstrated a number of tympanograms that did not conform to the A, B, or C classification. In these tympanograms the peak pressure was greater than -100 mm water with normal compliance (.1-1.5 cc); or the highest compliance measureable was at +200 mm water and gradually decreasing compliance was seen with decreasing pressure (Figure 1). These tympanograms are designated as type D (positive) tympanograms.

The initial tympanometry findings of 43 ear infections are presented in Table I. Forty-three percent of these initial examinations showed a Type D (positive) tympanogram, while 35 percent showed a type B or flat tympanogram. Nine percent showed a Type A tympanogram and 9 percent could not be tested. This was usually due to a poor air seal. Five percent of the ear examinations showed a type C tympanogram.

The sex distribution and mean age of the patients with these tympanograms were comparable. The tympanic membranes were described as bulging in 76 percent of the ears with type D (positive) tympanograms and in 64 percent of the ears with type B tympanograms.

Table II compares the initial tympanograms with outcome. Ninety-four percent (16 of 17) of the type D (positive) tympanograms had a successful outcome during the followup period; however, only 38 percent (5 of 13) of the type B (flat) tympanograms had a successful outcome during that same period. Among the tympanograms that failed to return to normal in the followup period, 80 percent (8 of 10) were initially type B (flat). When outcome was compared to initial tympanometry, a significantly poorer outcome was noted after type B tympanograms ($p = < .005$).

There were no significant differences in outcome when patients who received the placebo were compared to those who received the antihistamine/decongestant (Table III). The mean age and sex distribution of the two treatment groups was similar. Twenty-three percent of patients given triprolidine/pseudoephedrine failed to improve during the followup period, and 27 percent of patients given placebo failed to improve during the same followup period. Type P (positive) tympanograms and type B tympanograms were randomly distributed among the patients receiving the antihistamine/decongestant and the placebo. Among the nineteen patients receiving the placebo, nine had type P tympanograms and six had type B tympanograms.

Positive pressure tympanograms with the maximum compliance at +200 mm water or greater and a gradually decreasing compliance with decreasing pressure have not been noted or classified previously.

Tympanograms with positive pressure peaks are a rarely observed finding. Paradise et al compared tympanogram types with otoscopic diagnosis and classified three percent (7 of 273) of the tympanograms as HP (High Positive Pressure).

Groothuis et al made no mention of positive tympanograms among a group of 43 infants who had tympanograms obtained during their first attack of otitis media. Eighty-seven percent of the tympanograms were type B, six percent were type A (shallow) and seven percent were type C. Abnormal tympanograms persisted for six months in 63 percent of the examinations. The patients in the study by Groothuis et al were younger than the patients we studied, suggesting that infants may not show a positive tympanogram with otitis media.

The results of our study demonstrate the association of significantly poorer outcome in patients with acute otitis media and a type B (flat) tympanogram when compared to patients with acute otitis media and a type P (positive) tympanogram. No differences in outcome were noted among patients receiving the antihistamine/decongestant and patients receiving placebo.

Tympanometry at the time a diagnosis of acute otitis media is made does have prognostic value; this technique identified a group of patients that need particularly careful followup, i.e., patients with type B (flat) tympanograms.

POSITIVE TYMPANOGRAMS

TYPE HP

TYPE P

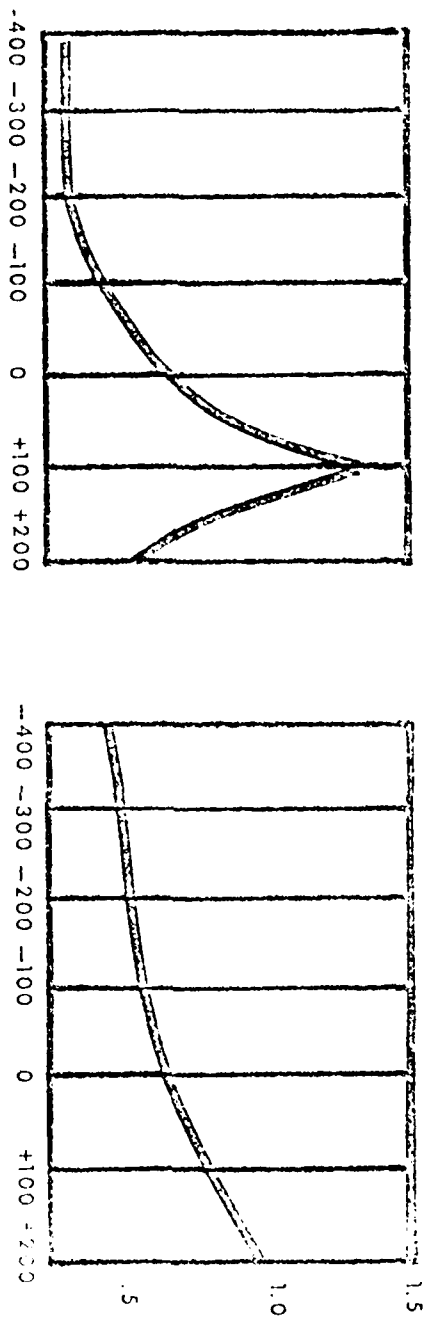


FIGURE 1

TABLE 1

TYMPANOMETRY IN EARLY OTITIS MEDIA
(43 Ear Examinations)

<u>Tympanogram</u>	<u>Number (Percent)</u>		<u>Male</u>	<u>Female</u>	<u>Mean Age (Months)</u>
P	18	(43)	10	8	64
B	15	(35)	10	5	54
A	4	(9)	3	1	58
CNT	4	(9)	2	2	36
C	2	(5)	0	2	78
Total	43	(100)	25	18	58

CNT = could not test

TABLE II

INITIAL TYMPANOMETRY AND OUTCOME AFTER SIX WEEKS

<u>Initial Tympanogram</u>	<u>Number</u>	<u>Outcome</u>		<u>No Follow-Up</u>
		<u>Success</u>	<u>Failure</u>	
P	18	16	1	1
B	15	5	8	2
A	4	2		2
CNT	4	3	1	
C	2	1		1
Total	43	27	10	6

CNT = Could not test

χ^2 P vs B, $p = <.005$

TABLE III

PATIENTS RECEIVING ANTIHISTAMINE/DECONGESTANT
OR PLACEBO AND OUTCOME

<u>Drug</u>	<u>Number</u>	<u>Outcome</u>		<u>No Follow-Up</u>
		<u>Success</u>	<u>Failure</u>	
Tripolidine Hydrochloride/ Pseudoephedrine	13	10	3	
Placebo	19	11	4	4
Total	32	21	7	4

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Detection of Bacterial Antigen in Body Fluid by Counterimmuno-electrophoresis

WORK UNIT NO: 77/05

PRINCIPAL INVESTIGATOR LTC R Lampe MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the presence of bacterial antigen in various body fluids detected by counterimmuno-electrophoresis (CIE) to standard bacteriologic methods of identification.

TECHNICAL APPROACH

Pediatric patients suspected of having a bacterial infection will have appropriate Gram stains and cultures performed. In addition, sera, urine, and the body fluid suspected of being infected will be studied using CIE with the following antisera: Pneumococcal antisera, Haemophilus influenza B antisera, Neisseria meningitidis antisera and Staphylococcal antisera. Should a specific antigen be detected, this will be followed sequentially during the hospitalization. The withdrawal of body fluids for this study will only accompany clinically indicated procedures requiring fluid withdrawal for diagnostic purposes.

CONSUMABLE SUPPLIES

\$117

PROGRESS

Over 400 clinical specimens (CSF, serum, urine, pleural fluids, exudates) have been analyzed to date. The results have been summarized for presentation to the Uniformed Services Pediatric Seminar:

Counterimmuno-electrophoresis using commercially available antisera against Haemophilus influenza B, pneumococcus and Group B Streptococcus was initiated to evaluate this technique's usefulness at a military teaching hospital. Over 400 specimens including sera, cerebrospinal fluid (CSF), urine, pleural fluid and joint fluid were studied.

H. influenzae b antigen was detected in CSF, sera and pleural fluid. Among patients with culture positive meningitis due to H. influenzae b, antigen was detected in six of seven CSF specimens (86%). Among patients with H. influenzae b bacteremia, antigen was detected in three of seven (43%). There were two patients, one with meningitis and one with empyema, whose cultures were negative but had H. influenzae b antigen in CSF and

pleural fluid, respectively. Both patients had received antibiotics before cultures were obtained.

Pneumococcal antigen was detected in either CSF, sera or pleural fluid of six patients. There were three patients, one with pneumonia and two with empyema, whose initial cultures were negative but who had pneumococcal antigen in sera or pleural fluid. The two patients with empyema had received antibiotics before cultures were obtained.

There were five neonates who had group B streptococcal antigen detected in either CSF, pleural fluid or urine. In two patients, bacterial cultures were negative.

Using staphylococcal antisera prepared at our institution, staphylococcal antigen was detected in the pleural fluid of one patient with a Staphylococcus aureus empyema, and antigen was detected in the joint fluid of another patient with a septic knee and tibial osteomyelitis secondary to S. aureus. There were no cross reactions with this antisera and other clinical specimens positive for H. influenzae b, pneumococcal or group B streptococcal antigens. This antisera was able to detect 0.3 mg of purified teichoic acid from S. aureus.

Counterimmunoelectrophoresis using commercially available antisera was useful in the detection of antigens from H. influenzae b, pneumococcus or group B Streptococcus. It was particularly helpful in patients with prior antibiotic therapy. Representative examples of its value in empyema patients will be presented. The detection of staphylococcal antigen (teichoic acid) with prepared antisera appears promising.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Zinc Levels in Maternal Infant Pairs

WORK UNIT NO: 77/10

PRINCIPAL INVESTIGATOR LTC L.L. Penney, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the zinc level in maternal-infant pairs and to see if there is a correlation with the incidence of infection.

TECHNICAL APPROACH

Zinc and phosphate concentrations in maternal and neonatal cord blood will be correlated with the incidence of neonatal sepsis in a blind retrospective study. The hypothesis of increasing zinc and phosphate levels in enhanced amniotic fluid bactericidal activity will be studied

CONSUMABLE SUPPLIES

\$179

PROGRESS

Over 1000 samples have been analyzed. Statistical correlation of the data is continuing but is slowed due to inability to retrieve patient records.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Investigation of the Effects of Diphenylhydantoin on Intellectual Functioning of Children

WORK UNIT NO: 77/13

PRINCIPAL INVESTIGATOR LTC P. F. LoPiccolo, MD

ASSOCIATE INVESTIGATORS: CPT Robert Hulsebus, PhD

OBJECTIVES

To determine if Dilantin has any effect on intellectual functioning.

TECHNICAL APPROACH

To test children over the age of six years who have been placed on phenobarb or dilantin because of a new seizure disorder. To test children who have been on long term anticonvulsants to see if there has been any change in intellectual function. This can only be accomplished if children had educational and psychological evaluations before the onset of their seizure disorder. Testing is being accomplished by Psychology using the WISC-P. The first part of the study has gone slowly because we have had very few cases of new spontaneous seizure disorders in children over the age of 6 years.

PROGRESS

Due to lack of support individuals this project has been temporarily suspended. I hope with the start of the Child Development Fellowship - to be able to continue.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Infant Parent Bonding and Its Relationship to the Healthy
Resolution of Grief

WORK UNIT NO: 77/18

PRINCIPAL INVESTIGATOR Vivian Sheliga LT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To evaluate our current inpatient and outpatient nursery services and to increase our help to families who experience the death of a newborn. We were particularly interested in how absence of "normal" bonding affects the grief reaction.

TECHNICAL APPROACH

Eighteen families were interviewed, half in hospital, half in homes. Two interviewers of the three on the team saw each family. Interviews were geared to a specific set of questions and all were taped when permission was given by family. Family previously had been asked to complete a brief questionnaire containing some of the same questions as interview.

PROGRESS

Many factors have been delineated as contributing to the prolongation of parental grief following the death of a newborn, with most of the factors identifiable as areas which more sensitive hospital personnel could help alleviate. Some of the preliminary findings were incorporated by our social workers into routine operational guidelines. The principal investigator has been reassigned.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Breast Feeding Survey

WORK UNIT NO: 77/21

PRINCIPAL INVESTIGATOR

CPT Jackson ANC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

Evaluate effectiveness of current breast feeding teaching program at this hospital. Determine breast feeding population and reason for decision to do so.

TECHNICAL APPROACH

Mothers visiting the Well Baby Clinic will be administered a questionnaire on several successive visits to determine the number of breast feeding mothers, non-breast feeding mothers and/or discontinued breast feeding mothers. Data will be analyzed attempting to identify factors which encourage or discourage mothers from breast feeding.

PROGRESS

The principal investigator has been reassigned. No progress was reported.

STATUS: Terminated

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Maintenance of Patency of the Ductus Arteriosus in Congenital Cardiac Lesion

WORK UNIT NO: 78/14

PRINCIPAL INVESTIGATOR MAJ Wm Pearl, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To maintain patency of the ductus arteriosus in infants with congenital heart disease, by infusing prostaglandin until diagnostic studies are completed and surgery can be arranged.

TECHNICAL APPROACH

Prostaglandin F is the only nonsurgical treatment available for treatment of certain congenital heart defects such as maintaining patency of the ductus arteriosus until cardiac abnormalities in newborn infants can be surgically corrected. In infants in whom blood is flowing through the ductus from the aorta to the pulmonary artery, a catheter will be placed through the umbilical artery to the first part of the descending aorta, at or just above the ductus. Prostaglandin F₁ will be infused continually into this region at the rate of 0.1 micrograms per kilogram per minute. In infants in whom blood flow is passing through the ductus from the pulmonary artery to the aorta, a catheter will be placed in the pulmonary artery just beyond the ductus arteriosus, and the Prostaglandin F₁ will be infused at the rate of 0.1 micrograms per kilogram per minute. In the event that the major artery cannot be catheterized, the infusion will be given into a large vein, and the investigator will be asked to observe the infant closely for any systemic effects. The infusion will be continued until surgery can be performed; this will usually be in a matter of hours. If the infusion is to be continued for more than seven days, the investigator should contact the monitor.

PROGRESS

The annual review of this protocol was conducted by the WRAMC Human Use Institutional Review Committee 26 Jul 79. At that time six patients had been treated. The only recognized side effect or complication was blistering and vasodilatation at the injection sited.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Penicillin Alone vs Ampicillin and Gentamicin in the Treatment of Group B Streptococcal Sepsis

WORK UNIT NO: 78/15

PRINCIPAL INVESTIGATOR: MAJ R. Heath, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the in vivo and in vitro killing rates of these antibiotics.

TECHNICAL APPROACH

Scintillation counting will be used for in vitro studies. Serial blood cultures will be used for in vivo studies with a rabbit model.

CONSUMABLE SUPPLIES

\$922

PROGRESS

Group B streptococci have been shown to be relatively resistant to loss in colony forming units during short term exposure to penicillin doses 1000 times greater than the minimal inhibitory concentration (MIC). In Todd Hewitt Broth supplemented with 100 ug of the antibiotic per ml, the number of colony forming units decreases only 70% in three hours. During this time, the cells do not lyse as determined spectrophotometrically and the maintenance of H₃ labelled DNA intracellularly. Conversely, there is a loss in C14 glycerol labelled cell wall components.

In in vivo experiments using a rabbit model, penicillin treated Group B streptococci were cleared from the blood stream more slowly than untreated cells. This difference was not seen in rabbits immunized with a nonhomologous serotype.

Despite the loss in cell wall material after a 3-hour penicillin treatment, there were no differences in the in vivo response of rabbits to intravenous injections with cell suspensions. The febrile response and drop in white blood cells seen immediately post-injection

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Efficacy of Intravenous and/or Intraventricular
Antibiotic Therapy of Gram Negative Meningitis

WORK UNIT NO: 78/16

PRINCIPAL INVESTIGATOR MAJ R. Heath, M.D.

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine which of the above methods of antibiotic administration results in the more rapid sterilization of infected ventricular fluid.

TECHNICAL APPROACH

Dogs will have E. coli instilled directly into their ventricles. Antibiotics will be given intravenously or intramuscularly + intraventricularly, or intraventricularly alone, and serial culturing done for bacterial growth.

PROGRESS

Recent human data has been published which answers this question. No further study is contemplated.

STATUS: Terminated

THIS REPORT IS A SUMMARY OF THE RESULTS OF THE STUDY

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: The Efficacy of Active Immunization to Group B Streptococcal
(GBS) Organisms in Preventing GBS Sepsis

WORK UNIT NO: 78/22

PRINCIPAL INVESTIGATOR MAJ R.E. Heath, M.D.

ASSOCIATE INVESTIGATORS: Robert Frederick, PhD

OBJECTIVES

To determine if active immunity will prevent acquisition of disease and/or prevent and/or blunt the clinical parameters of sepsis.

TECHNICAL APPROACH

A rabbit model is being used in this study. Rabbits are immunized with GBS until they have a "+" CIE to GBS antigen. Once a "+" titer is demonstrated, the animals are injected with both live and killed organisms. CBCs, blood gases, and temperatures are followed closely. If death occurs, histological examination of tissue will be performed.

CONSUMABLE SUPPLIES

\$1623

PROGRESS

The model works very well, and the project is approximately one-half complete, currently investigating what antibody fraction offers protection. A presentation to the Pediatric Triservice Seminar, San Diego, CA, Mar 1979 is summarized below:

By far the greatest efforts involved in the study of the immunologic circumstances of group B streptococci have centered around the type specific antigens, almost to the exclusion of non-type specific antigens such as the group B carbohydrate. In preliminary studies in rabbits, however, we noted a marked protection against a group B type Ia challenge when the animals had been immunized with a type III strain. These experiments were repeated as described above, using an immunization regimen that reportedly maximizes anti-group B (Q10) activity while minimizing anti-type specific activity. The effectiveness of this regimen was tested using several techniques and antigen preparations. Very few rabbit sera had any anti-type III detectable activity, and there were no demonstrable cross-reactions with type Ia native or core antigen preparations. While the sensitivity of these tests could be greater, by using radioimmunoassay for example, it seems unlikely that such low titers would be protective.

This protection could not be reproduced by immunizing with the "type-less" strain, 090R. The reason for the lack of protection seen in these rabbits is not known. There were no obvious differences in antibody titer to the group Q10 suggesting that the group specific Q10 was not the protective antigen; however, Baker has noted the possibility of a fundamental difference in the composition of the group carbohydrate in 090R and other type strains. If some other antigen is intimately involved, it may be that it is presented to the immunological system in different fashions by the type III and a genetically altered, 090R strain. Regardless of the mechanism, it does not appear that type specific immunity is involved in the protection reported here.

Previous reports indicate that rabbit antisera to the group B specific cell wall polysaccharide do not protect mice from the lethal effects of an organism challenge. Opsonophagocytic studies with Group B specific antisera demonstrate some ability to kill types Ia, Ib, and Ic organisms; however, this antisera was shown not to interact with type II or type III organisms. Anthony found that rabbit antisera to type III Group B streptococcus did not opsonophagocytize type Ia bacteria. The group B specific polysaccharide is a known shared antigen assumed to be of no clinical significance. Several reports have discussed the presence on all serotypes of Group B streptococci of a protein moiety. Known as X and R, one of these antigens, but not both, is reported to be on each strain. The importance of these antigens is currently not known.

The phenomenon of cross-reactive protection has been demonstrated in several ways, but whether this is occurring here has not been absolutely excluded. Perhaps with further refinement of the immunizing preparation and the challenge organism, the immunizing process, this may be resolved.

It is important to note that the immediate physiologic changes that occur after i.v. administration of group B streptococcal suspensions were not suppressed by the immunization procedure. This suggests that these parameters may not be associated with the precipitating event in the rabbit fatalities and consequently are of little diagnostic value in evaluating the prognosis of the infected animal. Perhaps then, it may be more pertinent to critically examine the events leading up to or occurring immediately prior to the time the animal expires. Such studies are currently under way in our laboratory.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Detection of Toxin by the Group B Streptococcal (GBS)
Organism

WORK UNIT NO: 78/23

PRINCIPAL INVESTIGATOR MAJ R.F. Heath, M.D.

ASSOCIATE INVESTIGATORS: Robert Frederick, PhD

OBJECTIVES

To determine if the GBS organism has evidence of producing a toxin.

TECHNICAL APPROACH

Live and killed organisms will be injected into rabbits. CBCs, blood gases, and temperatures will be followed closely. Necropsy specimens will be histologically reviewed.

CONSUMABLE SUPPLIES

\$3049

PROGRESS

We have demonstrated similar changes in all parameters with both live and killed organisms indicating a high probability of toxin production by GBS. Isolation and purification studies are continuing. An abstract from a presentation at the Annual Meeting of the Society for Pediatric Research, Atlanta, Georgia, April 1979 describes our work further:

Three groups of rabbits were intravenously (IV) injected with either live GBS organisms, killed organisms, or saline. Animals in both treatment groups exhibited lethargy, weakness and labored respirations; death occurred in 19/19 who received live organisms and in 4/15 who received killed organisms. The 16 control animals remained asymptomatic. Each animal had rectal temperature, blood gas determination, white blood cell count, and platelet count performed before treatment and at 1, 2, 4, 8 and 24 hours (hrs).

The live organism group experienced hyperthermia ($p < .05$) at 4 hrs; hypothermia at 34 hrs. ($p < .05$); leukopenia at 2, 4, 8 and 24 hrs. ($p < .01$); metabolic acidosis at 8 and 24 hrs. ($p < .05$); and thrombocytopenia at 24 hrs. ($p < .05$). The killed organism group demonstrated hyperthermia at 2, 4 and 8 hrs. ($p < .05$); hypocarbia at 1, 8 and 24 hrs. ($p < .05$ - $p < .001$); and metabolic acidosis at 2 hrs. ($p < .05$). Histological review of lung specimens from both groups revealed identical pulmonary changes which were analogous to those reported to occur in neonatal GBS disease. Because similar clinical, laboratory, and histological changes were induced with live and killed organisms, we postulate that a toxin is operative in early onset GBS disease. The IV administered organisms produced histological changes indistinguishable from those described to occur in neonates where organisms are presumed to be acquired by the aspiration of infected amniotic fluid.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

Antibiotic Prophylaxis for Recurrent Otitis Media: Comparison of
TITLE: Sulfasoxizole, Erythromycin, and Placebo

WORK UNIT NO: 78/25

PRINCIPAL INVESTIGATOR: LTC M. Weir, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the effect of chronic administration of oral sulfasoxizole, erythromycin or placebo has upon the number of ear infections in children with a history of recurrent otitis media.

TECHNICAL APPROACH

Children under the age of six years who, upon review of their outpatient chart, have a documented history of four or more ear infections in the preceding twelve months will be considered eligible for the study. Children with previous history of PE tubes, cleft palate or immune disease will be excluded. After informed parental consent, the children will be placed on either sulfasoxizole 25 mgm/kg/dose b.i.d. erythromycin 10 mgm/kg/dose b.i.d., or placebo for a three-month period. During this time the patient will be followed monthly with impedance tympanometry and physical examination. Any new ear infections during this period will be treated with systemic antibiotics for ten days. During the second and third three-month period an alternate drug will be used. Each patient will be followed for nine months and will serve as his or her own control. (Three months on Sulfasoxizole, 3 months on placebo, 3 months on erythromycin) in random order. At the conclusion of the study, the frequency of ear infections in children receiving placebo will be compared to those receiving sulfasoxizole or erythromycin.

PROGRESS

The principal investigator was reassigned and has been replaced by Dr. Weir. No patients were entered in FY79 as final approval was not received until after the FY80 season.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Measles, Mumps and Rubella Immunity in Military Adolescent
Dependents; Correlation with Immunization History

WORK UNIT NO: 79/12

PRINCIPAL INVESTIGATOR MAJ A. Butler, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the number of adolescents with serologic immunity to measles, mumps, and rubella and to correlate this with their immunization/disease history.

TECHNICAL APPROACH

In September 1978 U.S. Army Health Services Command requested an immunization survey be conducted to determine the adequacy of the Army Medical Department dependent immunizations. The impetus for this survey was the Presidential Childhood Immunization Initiative and encouragement from the Surgeon General's Office. The occurrence of large numbers of measles cases in junior and senior high school students has highlighted the need to assess the immunization status of children particularly in the adolescent age group and to provide immunization to those not known to be protected. Nearly one-half of the reported cases of measles occur in teenagers and fifty percent of reported fatalities from measles occurred in adolescents. At the present time there are only limited data relating to the actual antibody status of a major segment of the population. For obvious reasons we propose to determine serologic immunity to measles, mumps, and rubella and to correlate this information with their disease or immunization history.

Each year in May and August one day is set aside for school and sports physical examinations for dependent children at William Beaumont AMC. Approximately six hundred children are examined on these days. Sera have been collected from one hundred and thirty adolescents, after verbal consent, and a history of their immunization record of measles, mumps, or rubella immunization or disease was obtained. Serologic tests including hemagglutination inhibition titers to measles, neutralization antibody to mumps, and hemagglutination inhibition titer to rubella will be performed with the assistance of LTC R McScott, MC, Dent Virology, WRAIR, Wash DC. Titers less than 1:4 will indicate susceptibility, greater than 1:4 will indicate immunity. These data should provide the proportion of our adolescent population that have serologic immunity to measles, mumps and rubella and indicate the reliability of the history obtained from the patient's immunization record.

PROGRESS

Depending on the category 30-50% of the first set of specimens revealed a non-immune status. Only a small percentage of collected samples have been analyzed.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEALMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Infant Auditory Discrimination of Parents and Strangers

WORK UNIT NO: 77/12

PRINCIPAL INVESTIGATOR Robert C. Hulsebus, PhD, CPT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of this research was to determine the extent to which very young infants are able to discriminate parents from strangers of the same sex; the present protocol involved comparison between fathers and male strangers.

TECHNICAL APPROACH

Parents are to be contacted within 1-2 days of birth and the planned research will be briefly described. Those who express interest in the study will be contacted approximately one week later and will be given a consent form. For each comparison (father's vs male stranger, and mother vs father) the reaction of 12 - to 15 infants between 1 and 2 weeks of age will be compared.

PROGRESS

There were results from 20 infants which met the criteria of sufficient crying and of sufficient pausing while the adults were speaking to the infants. The major comparison of interest was the extent to which infants would pause from crying more readily to their father's voices than to a male stranger's voice. (Earlier published research revealed that infants discriminated their mother's voices from female stranger's voices and paused significantly sooner when their mothers spoke). Two scorers worked independently and simultaneously to transcribe on an event recorder the pattern of cries and pauses emitted by each infant and to each adult. The percent agreement as to which adult the criterion pause occurred first was calculated; in 23 of 24 cases there was agreement - for a 95% rate of agreement. The latencies to criterion pauses for father and stranger were compared by means of t-tests for paired comparisons. The results were as follows: $t = 2.925$, $p < .01$, a highly significant difference in favor of the fathers. Thus, the infants paused significantly sooner when their fathers spoke to them supporting the conclusion that infants with an average age of 2 weeks can and do differentiate their father's voices from strangers' voices. This

Work Unit 77/12

finding is consistent with the aforementioned results reported with mothers and their infants. Together these studies shed new light on the as yet not fully understood period of early infancy and the beginning of social attachment. These data have been submitted for publication.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

The Effect of Instructional Pretraining and Type of Treatment on the Acquisition of Assertive Behavior

WORK UNIT NO: 78/04

PRINCIPAL INVESTIGATOR Edward O. Crandell, LT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The purpose of the study is to compare the effectiveness of two methods of psychotherapy (behavioral and insight-oriented) used in conjunction with instructional retraining on development of assertive behaviors.

TECHNICAL APPROACH

A total of 50 volunteer subjects will be selected from among the patient population of the Psychology Service of William Beaumont Army Medical Center in El Paso, Texas. All subjects will be assigned to one of five groups. The purpose of these groups will be to aid each subject in his/her ability to behave assertively and to determine which of the five methods to be used is most effective in teaching this skill. The procedures to be followed and qualifications of the therapists to be used are described in detail in the originally submitted protocol.

PROGRESS

The study investigated the effect of behavior therapy, insight-oriented therapy, and instructional pretraining on the acquisition of assertive behavior. The dependent variables were the expression of positive assertive statements, the expression of negative assertive statements, and the predisposition to respond assertively. The independent variables of type of treatment and type of pretraining were combined in a completely randomized 2 x 2 multifactor design with a fifth group added which received instructional pretraining only. It was hypothesized that subjects receiving behavior therapy plus instructional pretraining would score significantly higher on behavioral and self-report measures of assertion immediately after treatment and 30 days following treatment.

A total of 40 subjects were randomly assigned to one of the five groups, and treatment and control procedures were randomly assigned to the groups. The subjects were post-tested immediately after treatment and 30 days following treatment using behavioral measures of positive and

negative assertion and a self-report measure of assertion. The behavioral measures consisted of a positive assertion score and negative assertion score obtained from the independent ratings of the subjects' responses to videotaped situations and written statements requiring the expression of positive and negative assertion. The self-report measure was the Adult Self-Expression Scale.

Behavior therapy consisted of modeling, feedback, and behavior rehearsal using videotaped assertive problem scenes. Insight-oriented therapy consisted of the identification of assertive problems and the exploration of feelings through the use of empathic responses by the therapists. All treatment was administered individually in four sessions which occurred within two weeks of pretraining. The instructional pretraining procedure consisted of a videotaped presentation containing instructions about the components of assertive behavior and assertive responses. Examples of assertive response were modeled. Subjects receiving only instructional pretraining viewed the videotaped presentation and were post-tested two weeks later.

Results of univariate ANOVA revealed a significant difference ($p < .01$) among the five groups on the negative assertion score obtained from the videotaped measure immediately following treatment. ANOVA tests for the other dependent measures were statistically non-significant. Multiple comparisons of the negative assertion mean scores on the videotaped measure using the Scheffe procedure resulted in a significant difference between groups which received behavior therapy and those receiving insight-oriented therapy. Subjects who received behavior therapy made significantly more negative assertions on the videotaped measure. The influence of instructional pretraining was found to be nonsignificant. Analysis of the assertion scores on the written statements and the Adult Self-Expression Scale resulted in no significant differences among the groups immediately after treatment and 30 days following treatment.

The hypothesis that the combination of instructional pretraining and behavior therapy would result in significantly higher scores on the behavioral and self-report measures was not supported. The independent variable which contributed to higher negative assertion scores was the type of treatment received. Subjects receiving behavior therapy made significantly more negative assertive statements on the videotaped measure than subjects who received insight-oriented therapy or instructional pretraining only.

The results of the study supported the use of behavior therapy as a method of treating assertive problems. The use of an instructional pretraining component was not supported. The results questioned the need for specific training in positive assertion. The results were also seen as supporting the contention that behavioral measures are more effective discriminators of assertive behavior than self-report measures. It was recommended that future research examine the need for training in positive assertion and that the present study should be replicated using a no-treatment and no-pretraining control group.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUFORT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

FINAL REPORT

TITLE: Inventory Construction Attentional and Thinking Skill
Assessment for Children

WORK UNIT NO: 79/11

PRINCIPAL INVESTIGATOR: NAT Benjamin, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To improve our description of both normal and learning disabled childrens' attentional ability.

TECHNICAL APPROACH

Fifteen children diagnosed hyperactive/learning disabled by our Pediatric Department and fifteen children randomly assigned to attend regular classrooms and are diagnosed to be normal children will form the sample. A task with three different parts will be used to provide a score for each of the specific skills mentioned previously. A modified card sorting task will provide information concerning the child's distractibility, flexibility of attention, and degree of concentration. A stimulus familiarization task will be used to index the child's distractibility and the breadth of attention. A modified version of a vigilant task will be used to indicate the child's distractibility, ability to maintain an attentional set and the degree of concentration. This representation will permit the identification of those skill areas which are weak as well as the child's skills which are satisfactory. A followup study increasing the sample size will be proposed at a future date if significance is established in the current study.

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The proposed study has received the unanimous approval of the WAMC Clinical Investigations Committee. The work has been forwarded to the Department of the Army for approval has been achieved and permission to conduct the study has been received. If the proposed study is approved, it will be completed as soon as possible.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Development of a Computerized Trauma Registry

WORK UNIT NO: 76/09

PRINCIPAL INVESTIGATOR MAJ J.P. Collins Jr, MD, and William J Klenke 2LT, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To complete development of an automated system for storage, retrieval, and processing of pertinent data for patients with traumatic injury at VBAMC.

TECHNICAL APPROACH

A computer program will be written to allow the entering, editing, displaying, sorting, classifying and analyzing of patient information. The patients will be restricted to those who are admitted to the Trauma Ward. These records will be used to analyze the epidemiology of traumatic injury and the effectiveness of therapeutic modalities in the management of injured patients.

PROGRESS

The data and program will reside on the Hewlett Packard 9845 computer (property of the Clinical Investigations Service) and no longer on the IBM 1400 (Data Processing Branch). Data has been coded and saved on this older computer with no provision or ability to utilize the data. Data stored on the IBM 1400 will hopefully be transferred in a mechanical manner but it is most probable that the data will have to be re-entered manually. A temporary hire was accomplished by the Dent Surgery to enter patient data for 1979/1980 (data not entered on the IBM) to re-enter stored data if necessary, and to perform other administrative tasks in support of this trauma registry. The program, to be written by the Clinical Investigations Service, has been begun. The Clinical Investigations Service has also placed on MEDCASE 1980 an extension to the computer to facilitate the project. This equipment should be available late 1980.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUFORT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: An Investigation of the Effect of Supplemental Oxygen on
Chemically Induced Fat Embolization

WORK UNIT NO: 76/24

PRINCIPAL INVESTIGATOR: CPT Foret MD

ASSOCIATE INVESTIGATORS: CPT Hill MD

OBJECTIVES

To determine whether or not supplemental oxygen prevents or lessens the potentially lethal effects of chemically induced fat embolization in dogs.

TECHNICAL APPROACH

Clinical observations as well as lung scans are generally accepted as criteria for determination of the presence of fat embolism syndrome. In this study laboratory parameters and lung scans are obtained for a 5 day period in beagles following injection of oleic acid. This data is collected from dogs supported on either room air or supplemental oxygen.

PROGRESS

Animal testing was suspended temporarily in order to evaluate preliminary work for possible improvements in technique, including discontinuance of oleic acid for embolization.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Early Detection of Fatigue Fracture by Bone Scanning with Te-99
Bone Scan Agents

WORK UNIT NO: 76-51

PRINCIPAL INVESTIGATOR COL D.A. Vichick, MD
COL T.J. Scully, MD
ASSOCIATE INVESTIGATORS: MAJ H.A. Snowdy, MD

OBJECTIVES

To demonstrate if bone scans can detect fatigue fractures and/or stress reactions in bone in military personnel.

TECHNICAL APPROACH

Patients with suspected stress fractures of bone are given bone scans on a "stat" or "ASAP" basis usually the day after being seen by the orthopaedic physician.

PROGRESS

Part I of the project was investigating the clinical efficacy of bone scans to detect fatigue fractures or stress fractures. This concept was proven. Also the project found that bone scans would detect stress fractures two to four weeks before x-rays would confirm their presence. As a result the bone scan was found to be a very helpful diagnostic tool for the military orthopaedic surgeon. The bone scan would allow early confirmation of a potentially devastating process in military personnel. This was particularly helpful in stress fractures of the hip. This finding was a major importance to the orthopaedic community nationwide. Subsequently a preliminary report was given to the Society of Military Orthopaedic Surgeons in Washington, D.C. in November 1976. Locally a report was given to the New Mexico Orthopaedic Association in December 1976. At the conclusion of the study two reports were given to national professional societies. Final reports were given to the Western Orthopaedic Association in October 1977 and to a national meeting of nuclear medicine physicians in El Paso in the Spring of 1977. A written final report was published in October 1977, J Bone and Joint Surgery, which is the definitive national and international orthopaedic journal. At the present time Part II of the study is to be continued by the Orthopaedic Service. Part II is a study of the actual prevention of stress fractures in military basic trainees. COL Scully, Asst C, Orthopaedics, has instituted changes in the actual basic training cycle to prevent stress fractures. The number of stress fractures has decreased significantly since that program was introduced. The conclusion of the project will be publication or presentation of the results of the Part

Work Unit No: 76/31

II prevention program. Information available indicates a reduction from as high as 4.5% with overall stress fractures to a rate of less than 1/100. Furthermore, most stress fractures currently seen are associated with an underlying pathological condition.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Proposal for Joint Study by Orthopedic Service, Dept of
Clinics and Radiology

WORK UNIT NO: 76/32

PRINCIPAL INVESTIGATOR MAJ Ewart, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To compare the clinical entity of low back pain with the presence of radiographic anomalies of the lumbo-sacral spine.

TECHNICAL APPROACH

Group analysis in a prospective fashion taking into account high risk categories. Personnel undergoing separation physicals (retirement, etc) will be assessed radiographically for the presence of lumbosacral anomalies. This evaluation will be correlated with previous history and consultations for low back pain.

PROGRESS

Material was presented in a paper to the Society of Military Orthopedic Surgeons. It is of great interest that most anomalies occur in the same relative numbers in both the symptomatic and asymptomatic patient.

STATUS: Completed

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Pathophysiology and Treatment of Hemorrhagic and Traumatic Shock

WORK UNIT NO: 77/24

PRINCIPAL INVESTIGATOR MAJ J. Collins, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To study the pathophysiology and treatment of hemorrhagic and traumatic shock and the effect of vasodilation, steroids, and fibrinolysin on these types of shock.

TECHNICAL APPROACH

Disseminated Intravascular Coagulation (DIC) and fatality have been shown to require the presence of slow capillary flow (shock) and the presence of a thromboplastic material in the blood stream. It is proposed to test the efficacy of phenoxybenzamine (an alpha blocking agent), steroids, and fibrinolysin in the prevention of DIC following traumatic shock.

CONSUMABLE SUPPLIES

\$78

PROGRESS

Sixty animals have been studied to date. Although work was largely suspended in FY79, another principal investigator has assumed the protocol. A portion of the early results appeared in the first manuscript (Ann Surg 189:373, 1979) which is excerpted below:

Fourteen mongrel dogs were divided into two groups, A and F. The dogs were paired and a Group A dog and a Group F dog were done on adjacent tables at the same time. The designation as to group had been previously determined by the toss of a coin. Group A dogs were anesthetized with intravenous pentobarbitol and both femoral arteries catheterized, one for the recording of arterial blood pressure and the other for bleeding into a standard blood donor bag with sodium citrate. Two days previously 2 ml/kg of the dogs' blood had been withdrawn, anticoagulated with heparin and stored in a refrigerator. After catheterization of the femoral arteries, a 20 ml blood sample was taken and analyzed for 1) platelets 2) Prothrombin time 3) partial Thromboplastin time, 4) fibrinogen and 5) fibrin split products. Following this the previously withdrawn anticoagulated autologous blood was returned to the animal through the femoral artery catheter. The animal was then bled over a 15 minute period to a mean arterial blood pressure of 40 mmHg. Following this it was allowed to stabilize for 30 minutes during which time the mean arterial blood pressure usually rose from 40 mmHg to 60 or 80 mmHg. At the end of the stabilization period the animal was again bled to 40 mmHg per mean pressure over a 15 minute period. After this, the animal was kept at a mean arterial pressure of 40 mmHg for a one hour period by withdrawing small amounts of blood, or giving small amounts of normal saline intra-arterially. At the end of the hour period of shock a second blood sample was taken and analyzed as before. All the animal's blood was then restored by the intravenous route through a blood filter. The animal was observed for 24 hours. If the animal was alive at 24 hours, it was counted as a survivor.

Group F dogs were treated in a like manner except that the 2 ml/kg of heparinized blood which was withdrawn two days before the experiment, was frozen in dry ice, thawed, and then kept in a refrigerator until time for administration.

Of the 7 animals in Group A, none died. Of the paired seven animals in Group F, all died. This was plotted by the method of sequential sampling and the difference was found to be significant at the 5% level.

None of the animals in either the "A" or "F" groups had any fibrin split products before the shock. None of the animals in the "A" group showed any fibrin split products after the shock either. However, the mean level of fibrin split products after shock in the "F" group was 34 ug. This difference was significant($p < .01$).

Group "A" animals had a mean PTT of 19 seconds before shock. This increased to 34 seconds after shock. Group "F" animals increased significantly more, from 16 sec. to 127 seconds ($p < .05$)

Group "A" animals increased from 6.6 to 9.5 seconds a rise of 2.9 sec. Group "F" animals increased from 6.2 to 15.0 sec. an increase of 8.8 sec. This was significant ($p < .05$)

Platelet counts fell much more in the "F" group than in the "A" group (96 vs 32 thousand) but this was not significant.

The results would tend to indicate that a small amount (2 ml/kg) of hemolysis, harmless in itself, was enough to significantly increase mortality and coagulation changes characteristic of DIC, when the animals were in a state of hemorrhagic shock. Much more autogenous hemolyzed blood (10 ml/kg) given to 13 normal animals had no effect and produced no mortality.

It has been previously shown in a number of animal experiments that pure hemorrhagic shock is relatively harmless and easily reversible by saline or blood. In contrast, hemorrhagic shock complicated by tissue injury, exposure of the extracorporeal blood to air or mechanical injury, resulted in an irreversibility to treatment with IV fluids or blood and high mortality associated with coagulation changes characteristic of Disseminated Intravascular Coagulation (DIC). It was postulated that for DIC to occur, two separate conditions must be present: 1) A slow moving, acid, capillary flow (hemorrhagic shock) 2) a thromboplastic agent gaining access to the blood stream. These would include bacterial toxins, thrombin and lysed red cells. The thromboplastic effect of lysed red cells had been known for a long time. It may be a red cell thromboplastin discovered by Quick, or phospholipids liberated from the red cell or it may be merely the lysed cell membranes acting as particulate matter in the blood. Certainly it is not stroma-free hemoglobin, which is actually anti-coagulant, and which is harmless given intravenously. In the present experiments, hemorrhagic shock produced the slow capillary flow but resulted in no mortality and minimal coagulation changes. However, adding a small amount of lysed red cells to the slow capillary flow situation resulted in a high mortality and coagulation changes characteristic of DIC.

Hemolysis occurring in a normal blood flow is relatively harmless. Hemolysis occurring in a shock situation (slow capillary flow) may produce DIC and death.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: National Intraocular Lens Implantation Study

WORK UNIT NO:

78/03

PRINCIPAL INVESTIGATOR

COL S.M. Galas

ASSOCIATE INVESTIGATORS:

MAJ T.W. Doucet

OBJECTIVES

To participate in the study of clinical results of implantations of intraocular lenses organized by the Intraocular Lens Manufacturer's Association in response to directives of the Ophthalmic Classification Panel, FDA.

TECHNICAL APPROACH

An intraocular lens is a prosthetic replacement for the eye's crystalline lens. It is placed in the eye at the time of cataract surgery, where it is fixated by a variety of means, with the intention that it remain permanently and correct the large refractive error remaining after conventional cataract surgery.

PROGRESS

From 3 Oct 78 to 1 Jul 79 a total of 20 cataract removal surgeries with implantation of intraocular lens have been performed. All patients have been followed as outpatients as required by FDA. The SOP, as presented to the Clinical Investigations Committee, has been followed. There have been no undue complications except for one patient whose lens dislocated into the vitreous. The patient was referred to Brooke Army Medical Center for consultation and surgery was not recommended. Patient has been fitted with a contact lens and visual acuity is 20/25 in operated eye. There were no technical or surgical complications associated with this case. The lens dislocated approximately four months following surgery. We are now using Precision Cosmet anterior chamber lenses which cannot dislocate. These cases bring the total experience at WBAMC to nearly 60. Three previous complications were reported to the Human Use Committee 20 Feb 79 at the time of annual review and additional details are available in the minutes of that committee. Briefly these complications were usual and accepted with cataract surgery of any type. Based on these early observations, the procedure represents a significant advance in cataract treatment.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO TEXAS 79920

DETAIL SHEET

Compartmental Pressure Studies as a Determinant for the Need
TITLE: for Fasciotomy

WORK UNIT NO: 79/03

PRINCIPAL INVESTIGATOR: COL D. A. Vichick, MD

ASSOCIATE INVESTIGATORS: CPT K.F. Hill, MD; MAJ T.W. Fwart, MD

OBJECTIVES

Trauma (insult) to muscles will be followed by an injury reaction resulting in swelling (interstitial)(intercellular) of the involved muscle or muscles. If the traumatized muscles are contained within a nonyielding compartment, increased intracompartmental pressure can reach a level where it exceeds perfusion pressure (diastolic or venous pressure) although distal pulses may be present. As the pressure within the compartment approaches the systolic pressure of the patient, there is no tissue perfusion and the distal pulses are absent. Studies in dogs have shown that the tissue injury increases as the duration of the ischemia increases. The impedance of capillary flow and venous drainage will set a stage for increased swelling followed by increased venous blockage until the intracompartmental pressures can exceed the arterial pressure in the small vessels of the involved muscles. The state of ischemia caused by the increase in intracompartmental pressure can lead to necrosis and death of the involved muscles.

Clinical experience has demonstrated the ability to prevent muscle necrosis as a result of increased compartmental/intracompartmental pressure by performing a fasciotomy thus converting the closed and nonyielding space to an expandable area. The clinical parameters of compartment syndrome are: (a) Increased circumference of the extremity. (b) Increased pain of the involved area out of proportion to the injury and accentuated by voluntary motor effort. (c) Decreased motor power of the involved muscle group. (d) Decreased distal sensation. (e) Decreased quality of distal pulses.

The clinical criteria for a fasciotomy do not possess a high degree of sensitivity in indicating the necessity for fasciotomy. Thus errors of omission (delaying fasciotomy too long) and commission (performing fasciotomy when it is truly not needed) are still more frequent than desirable. It has been determined by Whitesides, et al., that as tissue pressure readings equal or exceed 50 millimeters of mercury, the patient must be carefully followed with periodic tissue pressure readings and monitoring of all signs and symptoms of a closed compartment syndrome. Further, as tissue pressures approach or equal the patient's diastolic pressure a fasciotomy is definitely indicated. Tissue pressures of 40-45 mm of mercury should usually be the upper limit prior to fasciotomy when the diastolic pressure is in the range of 70 mm of mercury. It was found that tissue recovery is essentially complete after four hours of ischemia, but only 50% complete after 6 hours of ischemia. The damage is extensive and irreversible after 8 hours of ischemia. The contained neurotissues

are even more sensitive to ischemia than muscle and thus the duration of ischemia is even more critical following prolonged increase of intracompartmental pressures.

A study will be conducted in which intracompartmental pressures of the anterior and posterior compartments of the legs, anterior and posterior compartments of the forearm, and dorsal interosseous compartments of the hand will be measured in various states of normal, stress and following disease or injury. The intracompartmental pressure values will be correlated with the clinical picture (pain, increased circumference, decreased motor activity and/or sensation, and quality of distal pulses). When possible and feasible, the uninjured extremity will be used as a control. During this study, fasciotomy will be performed using the accepted clinical indications without regard to the values as determined by the intracompartmental pressure studies alone.

TECHNICAL APPROACH

Three categories of patients will be tested, each group consisting of 25 but not more than 50 patients. The categories will be as follows:

Group 1 - Normal volunteers (or noninvolved extremities of Group 3 patients).

Group 2 - Volunteers who will perform strenuous physical activity with the involved extremity while compartmental pressures are monitored: before, during and after activity.

Group 3 - Volunteer patients who by way of disease or injury are suspected of having increased compartmental pressures of the lower leg, forearm, or dorsum of the hand.

A 22 or 24-gauge intracath will be inserted into the compartments to be studied or in question, both in the lower and upper extremity following a sterile preping of the area. The site selected for insertion will be determined by the investigator. The areas where muscle is felt to be compromised or to be normal will be primarily studied. Areas that closely surround fractures or known hematomas will be avoided if possible. The exact technique for recording intracompartmental pressures will be the same as described by Matsen et al. During the study, the compartment pressures will be obtained and correlated with the clinical picture, a determination will be made as to whether intracompartmental pressures offer a significant advantage in determining the need for fasciotomy over known clinical parameters.

The risk of the study to the volunteer participants is considered to be minimal and no greater than would occur with any intramuscular injection with a small bore needle.

PROGRESS

Approval from HSC had not been received by the end of the FY, 30 Sept 79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Effects of Tourniquet Ischemia on Systemic Coagulation Mechanism

WORK UNIT NO: 79/10

PRINCIPAL INVESTIGATOR: CPT K.J. Guidera, MC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

The objective of this study is to determine if there are any abnormalities of the clotting mechanism created secondary to an extremity being under tourniquet ischemia during surgery.

TECHNICAL APPROACH

The effect of surgical tourniquet ischemia has been investigated by multiple authors. Wilgis investigated the effects of this procedure on serum pH, pO₂, specific gravity and serum solids. Other authors such as Dahlback and Paletta have studied the histological changes in striated muscle when under such a tourniquet compression.

The specific purpose of this investigation is to determine whether an altered state of coagulation is being produced secondary to surgical tourniquet ischemia. Several tests will be done to include platelet counts, clotting times, fibrinogen levels, CPK isoenzyme levels, fibrin degradation product levels and in some cases measurement of clotting factor levels. In black patients, the sickling test will be performed.

The subjects of this study will be adult active duty, retired, and dependent patients undergoing elective hand surgery. Children and lactating or pregnant women will not be studied. No medication will be administered to these patients other than routine preoperative and intraoperative anesthetics. This study does not involve the use of medication. The patients will serve as their own controls. The phases of this investigation will include preoperative clotting studies, intraoperative venous blood samples while the surgical tourniquet is inflated, and postoperative plasma clotting studies. These samples will be evaluated while the patient is in the hospital and no further followup should be necessary. All data generated from the data will be standard hospital laboratory reports.

PROGRESS

HSC approval was received 29 Jul 79. No patients were entered in FY79.

STATUS: Ongoing

CLINICAL INVESTIGATIONS SERVICE
WILLIAM BEAUMONT ARMY MEDICAL CENTER
EL PASO, TEXAS 79920

DETAIL SHEET

The Incidence of Visual-Motor Perceptual Problems in Persons
TITLE: with Traumatic Hand Injuries

WORK UNIT NO: 79/42

PRINCIPAL INVESTIGATOR: MAJ M.J. Baker, MSC

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine if persons with traumatic hand injuries have pre-existing visual-motor perceptual problems which may have lead to their trauma.

TECHNICAL APPROACH

It is recognized by the Federal Government, school systems, and medical professionals that children may suffer from minimal brain dysfunction and/or developmental disabilities resulting in sensory-motor integration problems or inability to perform classroom and play activities in a manner appropriate for their age. In interviews of individuals with traumatic hand injuries it appears that these individuals may not know where their hands are in space and, therefore, suffer from a visual-motor perceptual problem, a form of sensory-motor integration.

The Slosson Drawing Coordination Test is reported "to screen out individuals suffering from serious forms of brain dysfunction or damage where eye-hand coordination is involved." "A reliability coefficient of .96 was obtained for a group of 200 individuals, aged 4 to 52 years." This test does not screen out individuals with emotional problems due to brain dysfunction nor does it identify individuals with eye-hand incoordination due to a specific visual-motor perceptual problem. The Kinesthesia Test of the Southern California Sensory Integration Test" is intended to measure the capacity to perceive joint position and movement." Although this test is standardized for individuals from 4 to 8 years of age, it is felt to be an indicator of individuals unable to perceive their extremities in space, that is, visual-motor perceptual dysfunction.

a. The specific purpose of this study is to determine if individuals with traumatic hand injuries also have a pre-existing visual-motor perceptual problem as measured by the Slosson Drawing Coordination Test and the Kinesthesia Test of the Southern California Sensory Integration Tests.

b. The number of subjects for the study will be 20 persons with traumatic hand injuries. The age range of these individuals will be 18 to 50 years of age; they will be active duty military, males and females.

c. The control group will consist of 20 individuals with no history of traumatic hand injuries or other perceptual problems. These individuals will be active duty military, males and females, with an age range of 18 to 30. The control group will be as close as possible in age and sex as the study group. This group will be expanded as needed to assure statistical significance.

d. Subjects for the study will be referred to Occupational Therapy by the Hand Surgery Service, WBAMC. Persons for the control group will be volunteers from the Troop Command, WBAMC. Other patients will not be used due to the possibility of their injury being the result of a perceptual problem.

Both study subjects and control group subjects will be given the Slosson Drawing Coordination Test and the Kinesthesia Test. The tests take approximately 20 minutes each to administer and will be scored according to the test protocols. The test results of individuals with traumatic hand injuries will be compared to the control group for determining significance.

PROGRESS

This study was not approved by HSC prior to the end of FY79.

STATUS: Ongoing

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CLINICAL INVESTIGATIONS SERVICE
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EL PASO, TEXAS 79920

DETAIL SHEET

TITLE: Perioperative Thrombosis Prophylaxis in Patients with
Peripheral Vascular Disease

WORK UNIT NO: 79/43

PRINCIPAL INVESTIGATOR: MAJ J.T. Collins, MD

ASSOCIATE INVESTIGATORS:

OBJECTIVES

To determine the efficacy and safety of low-dose heparin prophylaxis in patients undergoing peripheral vascular surgery.

TECHNICAL APPROACH

Patients entering the hospital for a proximal revascularization (aorto-iliac bypass, aorto-iliac endarterectomy, or aorto-femoral bypass) procedure will be randomly assigned to either a control or a treatment group. Patients in the control group will receive no thrombosis prophylaxis. Patients in the treatment group will receive 500 u of heparin subcutaneously each 13 hours for ten days after the methods of Kakkar and co-workers, and Flanc and co-workers. Heparin given intraoperatively will be reversed in keeping with our usual practice.

Venous thrombosis will be demonstrated using the 125I-fibrinogen leg scans. 125I-fibrinogen is converted to fibrin under the influence of thrombin, thus incorporating 125I into a developing clot.

Commercially available 125I-fibrinogen is a derivative of single-donor human plasma. These donors are carefully screened for blood borne, transmissible diseases, particularly hepatitis. No cases of hepatitis or other illnesses have been reported with the product to be used.

To perform the test, the freeze dried preparation is reconstituted with sterile water at the time of injection. A routine 1 cc dose consists of 2 mgm of clottable protein, and 140 mCi of 125I. All patients will receive 250 mg (5 drops) of saturated KI orally 24 hours prior to injection of 125I-fibrinogen to effect thyroid blockade.

125I decays by electron capture with a physical half-life of 60 days. There is no beta emission. Photons are of x-ray (35 KEV) and K x-ray (28 KEV).

External radiation is 1.5/mc/hr at 1 cm. Radiation dosimetry is as follows: thyroid (unblocked), 1.3 R/100 Ci; thyroid (blocked), 0.02 R/100 Ci; whole body, 0.02 R/100 Ci.

The administration of ¹²⁵I-fibrinogen and scintillation counting for each patient will be performed by the Nuclear Medicine Service, WBANC under the direction of Dr. H.W. Henry, MAJ,MC. The thrombus detector, to be purchased by the Clinical Investigations Service utilizes a thallium activated sodium iodide crystal. Counts will be taken daily beginning 24-hours after injection of the isotope and for a period of ten days unless an abnormal scan is noted. Therefore, the first dose will be given two days before operation.

The scanning procedure consists of passing the above described hand held device over the patients' sternum and at various levels of both lower extremities for periods of five to thirty seconds. Abnormal concentrations of ¹²⁵I in the lower extremities correlate well with deep venous thrombosis. The counting device is easily transported, the exam is quick and noninjurious to the patient, and it will be performed at the patients' bedside. ¹²⁵I-fibrinogen leg scanning is now a well accepted procedure in many hospitals.

Accurate documentation of all other thrombotic events will also be sought. Cerebrovascular accident will be diagnosed clinically and confirmation will be sought by vascular and statis brain scans. Suspected myocardial infarction will be confirmed by electrocardiogram and serial cardiac enzyme determinations. Patients who develop a positive ¹²⁵I-fibrinogen scan will have a phleborheogram performed daily. If the phleborheogram is positive, the case will be judged a failure of prophylaxis, and heparin will be begun by continuous infusion with the goal of keeping the activated partial thromboplastin time at 1.5 to 2.5 times normal. Phleborheography as developed by Cranley and co-workers has been confirmed by us to be 95.3% accurate for detecting clinically significant venous thrombi. Phleborheography is a noninvasive test with no risks to the patient. Suspected pulmonary embolism will be confirmed by chest x-ray, arterial blood gases, pulmonary scans, and pulmonary arteriography when indicated.

All patients will be counseled regarding the various ramifications of the protocol and will sign a human volunteer agreement prior to entry into the study. It is estimated that 100 patients will be entered into the protocol over a two-year period. Data concerning the perioperative management will be available at the end of two years. In the unlikely event that a patient with a contraindication or allergy to heparin should be considered for operation, he will be excluded from the study. Female patients, aged 15 to 50 years, will be screened with pregnancy tests and positive results will serve as a basis for elimination from this protocol.

Should a hemorrhagic complication develop, heparin administration will be discontinued. Although ecchymoses may develop at the site of heparin injection, the chance of developing wound hematomas or life threatening hemorrhage from low-dose heparin, properly administered, is essentially nil. A thrombin time will be obtained and circulating heparin will be neutralized by protamine if necessary. We will attempt to correlate the eventual outcome with the preoperative profiles.

PROGRESS

This study was not approved by OTSG prior to the end of FY79.

STATUS: Ongoing

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